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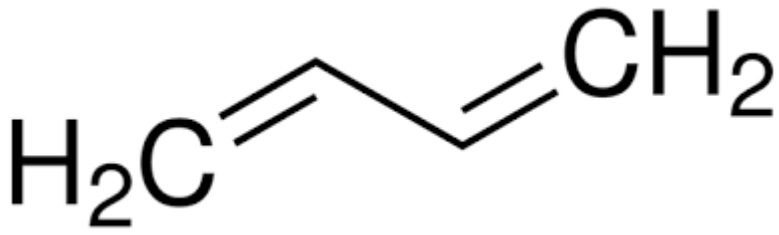
Office of Chemical Safety and
Pollution Prevention

United States
Environmental Protection Agency

Summary of and Response to External Peer Review and Public Comments on the Risk Evaluation and Technical Support Documents for 1,3-Butadiene



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Key Acronyms and Abbreviations

ACC	American Chemistry Council
ADAF	Age-Dependent Adjustment Factor
ADME	Absorption, Distribution, Metabolism, and Elimination
AEGL-1	Acute Exposure Guideline Level 1
AIHA	American Industrial Hygiene Association
AMTIC	Ambient Monitoring Technology Information Center
ANOVA	Analysis of Variance
AOP	Adverse Outcome Pathway
APF	Assigned Protection Factor
ATSDR	Agency for Toxic Substances and Disease Registry
BMC	Benchmark Concentration
BMCL	Benchmark Concentration Lower Confidence Limit
BMD	Benchmark Dose
BMDL	Benchmark Dose Lower Confidence Limit
BMR	Benchmark Response
CDR	Chemical Data Reporting
CEM	Consumer Exposure Model
CFR	Code of Federal Regulations
CML	Chronic Myeloid Leukemia
COU	Condition of Use
CWA	Clean Water Act
DDEF	Data Derived Extrapolation Factors
DEVL	Dermal Exposure to Volatile Liquids
DEB	1,2,3,4-diepoxybutane
DMR	Discharge Monitoring Report
EC	Effective Concentration
ECHA	European Chemicals Agency
ECRAD	Existing Chemicals Risk Assessment Division
EPA	U.S. Environmental Protection Agency
EU	European Union
HEC	Human Equivalent Concentrations
HED	Health Effects Division
HEM	Human Exposure Model
IIOAC	Integrated Indoor-Outdoor Air Calculator
IPCS	International Programme on Chemical Safety
IRIS	Integrated Risk Information System
IUR	Inhalation Unit Risk
LOAEL	Lowest-Observed-Adverse-Effect Level
LOD	Limit of Detection
MIE	Molecular Initiating Event
MLE	Maximum Likelihood Estimate
MMOA	Mutagenic Mode of Action
MOA	Mode of Action
MOE	Margin of Exposure
NASEM	National Academies of Sciences, Engineering, and Medicine
NCI	National Cancer Institute
NEI	National Emissions Inventory
NOAEL	No-Observed-Adverse-Effect Level

NTP	National Toxicology Program
OAR	Office of Air and Radiation
OECD	Organisation for Economic Co-operation and Development
OES	Occupational Exposure Scenario
OEV	Occupational Exposure Value
ONU	Occupational Non-User
OPPT	Office of Pollution Prevention and Toxics
ORD	Office of Research and Development
OSHA	Occupational Safety and Health Administration
PBPK	Physiologically Based Pharmacokinetic
PECO	Population, Exposure, Comparator, and Outcome
PEL	Permissible Exposure Limit
PESS	Potentially Exposed or Susceptible Subpopulations
POD	Point of Departure
PPE	Personal Protective Equipment
RMP	Risk Management Plan
SACC	Science Advisory Committee on Chemicals
SEG	Similar Exposure Group
SBR	Styrene Butadiene Rubber
STEL	Short-Term Exposure Limit
TRI	Toxics Release Inventory
TRV	Toxicity Reference Value
TSCA	Toxic Substances Control Act
TSD	Technical Support Document
TWA	Time-Weighted Average
UCMR3	Third Unregulated Contaminant Monitoring Rule
UF	Uncertainty Factor
U.S.	United States
WHO	World Health Organization
WQP	Water Quality Portal

Introduction

On December 3, 2024, the U.S. Environmental Protection Agency (EPA) published the 2024 *Draft Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2024g) and accepted public comment until March 20, 2025. Materials on the draft risk evaluation are available at www.regulations.gov in docket EPA-HQ-OPPT-2024-0425. A preparatory virtual public meeting was held on March 25, 2025, for reviewers and the public to comment on and ask questions regarding the scope and clarity of the draft charge questions for the Science Advisory Committee on Chemicals (SACC) peer review public meeting held from April 1 to 4, 2025.

This document summarizes all public and external peer review comments that the EPA's Office of Pollution Prevention and Toxics (OPPT) received for the draft risk evaluation of 1,3-butadiene, including all technical support documents (TSDs) and supplemental files in EPA-HQ-OPPT-2024-0425. Moreover, it provides EPA/OPPT's response to the comments received from the SACC peer reviewers, stakeholders and public, ensuring that all feedback is addressed equally. The document is organized by descending section and subsection headings (see also the Table of Contents). For example, Section 1.1.2.2, the first "1" refers a Summary of SACC Comments Organized by Charge Questions, the second "2" refers to Charge Question 1 - Environmental Exposure, the first "2" refers to Charge Question 1 part a.ii, and the second "2" refers to the second comment for that sub-question (1a.ii), and so on.

EPA/OPPT appreciates the valuable input provided by the public and peer review. The input resulted in revisions to the draft risk evaluation of 1,3-butadiene. In regard to responding to peer review comments, this response to comments focuses generally on the main bulleted recommendations provided by the SACC. The bulleted recommendations, generally, represent the most important consensus comments from the peer reviewers. Nevertheless, throughout the risk evaluation and this Response to Comments, EPA has addressed the issues raised by comments from all peer reviewers and public commenters.

Where appropriate, the peer review and public comments are categorized by the peer review charge questions. Additionally, within each theme comments that cover similar issues are presented together:

1. Overarching comments
2. Chemistry, fate, and transport of 1,3-butadiene
3. Releases and concentrations of 1,3-butadiene in the environment
4. Environmental risk assessment
5. Human health risk assessment
6. Unreasonable risk determination
7. Systematic review
8. Formatting and editing
9. Other comments on the draft risk evaluation
10. Comments not relevant to the draft risk evaluation

Table I-1. Index of Public Comment Submissions on 1,3-Butadiene Dockets, Sorted by Submission Number

Submission Number	Commenter Name
EPA-HQ-OPPT-2018-0451-0046	Sarah Amick/ U.S. Tire Manufacturers Association (USTMA)
EPA-HQ-OPPT-2018-0451-0049	Earthjustice et al.
EPA-HQ-OPPT-2018-0451-0050	Earthjustice
EPA-HQ-OPPT-2018-0451-0051	Earthjustice et al.
EPA-HQ-OPPT-2018-0451-0052	American Chemistry Council (ACC)
EPA-HQ-OPPT-2018-0451-0053	American Chemistry Council (ACC)
EPA-HQ-OPPT-2018-0451-0054	Ivan Rusyn
EPA-HQ-OPPT-2018-0451-0056	American Chemistry Council (ACC)
EPA-HQ-OPPT-2018-0451-0057	Environmental Defense Fund (EDF)
EPA-HQ-OPPT-2018-0451-0058	American Chemistry Council (ACC)
EPA-HQ-OPPT-2018-0451-0059	Washington State Departments of Ecology and Health
EPA-HQ-OPPT-2018-0451-0060	Environmental Defense Fund (EDF)
EPA-HQ-OPPT-2018-0451-0063	American Chemistry Council (ACC)
EPA-HQ-OPPT-2018-0451-0064	American Chemistry Council (ACC)
EPA-HQ-OPPT-2018-0451-0067	American Chemistry Council (ACC)
EPA-HQ-OPPT-2018-0451-0068	INV Nylon Chemicals Americas, LLC
EPA-HQ-OPPT-2024-0425-0052	American Chemistry Council (ACC)
EPA-HQ-OPPT-2024-0425-0053	American Industrial Hygiene Association (AIHA)
EPA-HQ-OPPT-2024-0425-0054	Temitope Asefon
EPA-HQ-OPPT-2024-0425-0055	Anto Lourdu Xavier Raj Arockia Selvarathinam
EPA-HQ-OPPT-2024-0425-0058	Nuclear Energy Institute (NEI)
EPA-HQ-OPPT-2024-0425-0059	Rachel Braaten
EPA-HQ-OPPT-2024-0425-0060	National Tribal Toxics Council
EPA-HQ-OPPT-2024-0425-0067	Celanese
EPA-HQ-OPPT-2024-0425-0068	Alliance for Chemical Distribution (ACD)
EPA-HQ-OPPT-2024-0425-0069	University of San Francisco Program on Reproductive Health and the Environment (UCSF PRHE)
EPA-HQ-OPPT-2024-0425-0073	Anonymous
EPA-HQ-OPPT-2024-0425-0076	American Chemistry Council (ACC)
EPA-HQ-OPPT-2024 -0425-0077	Household and Commercial Products Association (HCPA)
EPA-HQ-OPPT-2024-0425-0079	Environmental Defense Fund (EDF)
EPA-HQ-OPPT-2024-0425-0080	Dow Chemical Company
EPA-HQ-OPPT-2024-0425-0081	Boeing Company
EPA-HQ-OPPT-2024-0425-0082	U.S. Tire Manufacturers Association (USTMA)

Submission Number	Commenter Name
EPA-HQ-OPPT-2024-0425-0083	INV Nylon Chemicals Americas, LLC
EPA-HQ-OPPT-2024-0425-0084	American Fuel & Petrochemical Manufacturers (AFPM)
EPA-HQ-OPPT-2024-0425-0085	Alliance for Automotive Innovation
EPA-HQ-OPPT-2024-0425-0087	American Chemistry Council (ACC)
EPA-HQ-OPPT-2024-0425-0088	Beaver County Marcellus Awareness Community et al., (1 of 4)
EPA-HQ-OPPT-2024-0425-0089	Beaver County Marcellus Awareness Community et al., (2 of 4)
EPA-HQ-OPPT-2024-0425-0090	Beaver County Marcellus Awareness Community et al., (3 of 4)
EPA-HQ-OPPT-2024-0425-0091	Beaver County Marcellus Awareness Community et al., (4 of 4)
EPA-HQ-OPPT-2024-0425-0092	University of California, San Francisco Program on Reproductive Health and the Environment (UCSF PHRE)
EPA-HQ-OPPT-2024-0425-0100	Carlos Santos Burgoa/SACC Member
EPA-HQ-OPPT-2024-0425-0101	Christine Chaisson/SACC Member
EPA-HQ-OPPT-2024-0425-0102	Penelope Fenner-Crisp/SACC Member
EPA-HQ-OPPT-2024-0425-0103	George Cobb/SACC Chair
EPA-HQ-OPPT-2024-0425-0104	Chris Kirman/SciPinion, LLC
EPA-HQ-OPPT-2024-0425-0105	Veena Singla/Columbia University
EPA-HQ-OPPT-2024-0425-0106	MacKinsey Bach/ExxonMobil Biomedical Sciences, Inc.
EPA-HQ-OPPT-2024-0425-0107	Craig Warren Davis/Exponent
EPA-HQ-OPPT-2024-0425-0108	Paul DeLeo/American Chemistry Council
EPA-HQ-OPPT-2024-0425-0109	Neeraja Erraguntla/American Chemistry Council
EPA-HQ-OPPT-2024-0425-0110	Sylvia Maberti/ExxonMobil Biomedical Sciences, Inc.
EPA-HQ-OPPT-2024-0425-0111	Julie Panko/ToxStrategies
EPA-HQ-OPPT-2024-0425-0112	Alan Rovira/Shell Global Solutions Inc.
EPA-HQ-OPPT-2024-0425-0113	Alan Rovira/Shell Global Solutions Inc.
EPA-HQ-OPPT-2024-0425-0114	Dan Baker/Consultant
EPA-HQ-OPPT-2024-0425-0115	Jim Cooper/American Fuel & Petrochemical Manufacturers
EPA-HQ-OPPT-2024-0425-0116	University of California, San Francisco Program on Reproductive Health and the Environment
EPA-HQ-OPPT-2024-0425-0117	George Cobb/SACC Chair
EPA-HQ-OPPT-2024-0425-0118	American Fuel & Petrochemical Manufacturers (AFPM)
EPA-HQ-OPPT-2024-0425-0119	Rainbow Rubin/SACC member
EPA-HQ-OPPT-2024-0425-0120	Wendy Heiger-Bernays/SACC member
EPA-HQ-OPPT-2024-0425-0122	Veena Singla/Columbia University
EPA-HQ-OPPT-2024-0425-0125	American Chemistry Council (ACC)

1 Summary of SACC Comments Organized by Charge Questions

The 1,3-butadiene SACC recommendations and responses are summarized in the subsections below. The SACC meeting minutes, and final report are located at https://www.regulations.gov/document/EPA-HQ-OPPT-2024-0425-0123.

1.1 Charge Question 1 – Environmental Exposure

1.1.1 Charge Question 1a.i

1.1.1.1 Comment

Summary: The SACC provided two alternative recommendations for EPA to consider with respect to the break down products of 1,3-butadiene. As a bulleted recommendation on page 39 of the SACC report, the SACC emphasized the importance of considering potential risks from bioactive breakdown products of 1,3-butadiene, specifically formaldehyde and acrolein. They recommended conducting quantitative cumulative assessments that account for chemical combinations and co-exposures, even at low concentrations, focusing on carcinogens, mutagens, and reproductive toxicants collectively. They provided two references – Peng et al. (2022) and EPA-HQ-OPP-2007-0588-0140, which indicate the toxic effects of formaldehyde and acrolein on plants. Additionally, they shared three references– (U.S. EPA, 2009; Hohreiter and Rigg, 2001; U.S. EPA, 1987) which document the ambient water quality criteria for formaldehyde and acrolein.

Alternatively, the SACC recommended that EPA evaluate the environmental concentrations of 1,3-butadiene environmental transformation products (*e.g.*, acrolein and formaldehyde) and determine if a quantitative risk assessment is warranted. They suggested an alternative approach where chemical/ physical properties of both transformation products along with environmental chemical analysis and mass balance information could be used to help rule out the need for a quantitative assessment.

EPA Response: The SACC recommendations include two approaches to consider for the evaluation of breakdown products of 1,3-Butadiene. One approach emphasizes conducting quantitative cumulative assessments that account for chemical combinations and co-exposures, particularly focusing on carcinogens, mutagens, and reproductive toxicants, even at low concentrations. The alternative approach involves evaluating chemical/physical properties, environmental chemical analysis, and mass balance information, which could potentially negate the need for a quantitative risk assessment. Although a mass balance analysis has not be conducted, in the paragraphs below and in the *Physical Chemistry, Fate, and Transport Assessment for 1,3-Butadiene* (U.S. EPA, 2025f), EPA has critically considered the chemical and physical properties of 1,3-butadiene, formaldehyde, and acrolein and has determined that a quantitative assessment combining exposures of these chemicals is not necessary.

Data evaluated by EPA suggest that localized formation of the major transformation products from 1,3-butadiene, formaldehyde and acrolein, would not lead to a sustained or measurable increase in ambient concentrations beyond existing background levels. Therefore, secondary formation of formaldehyde and acrolein is not anticipated to significantly impact exposure or alter risk conclusions and these transformation products were not included in the risk assessment. There are three major reasons for this. Firstly, formaldehyde and acrolein are not uniquely attributable to 1,3-butadiene, as emissions from TSCA-regulated sources and other natural and anthropogenic activities, such as vehicle exhaust and secondary formation from other VOCs, far exceed the quantities that could reasonably be formed through atmospheric degradation of 1,3-butadiene released form TSCA facilities. Consequently, any incremental contributions from 1,3-butadiene photodegradation would be negligible relative to

environmental releases and background levels of formaldehyde (U.S. EPA, 2024a), rendering formaldehyde as a 1,3-butadiene degradate as not significantly impacting the risk characterization. Second, the atmospheric photodegradation of 1,3-butadiene involves complex radical-mediated pathways that are influenced by local photochemical conditions, including ambient concentrations of relevant radicals, sunlight intensity, temperature, and the presence of co-pollutants (Khaled et al., 2019; Vimal, 2008; Andersson and Ljungström, 1989). Any model-based estimation would entail considerable uncertainty and offer limited value for risk assessment purposes because it requires assumptions about prevailing environmental conditions, including concentrations of relevant radicals, temperature, and sunlight intensity. Third, both formaldehyde and acrolein undergo rapid photodegradation in the atmosphere, with half-lives typically measured in hours. Due to this rapid degradation, these compounds do not persist at measurable concentrations or accumulate in the environment and therefore do not impact risk characterization of 1,3-butadiene released from TSCA facilities.

A discussion of the major 1,3-butadiene degradants is included in Section 3.4.2 of the *Physical Chemistry, Fate, and Transport Assessment for 1,3-Butadiene* (U.S. EPA, 2025f). EPA reviewed the shared references ((Peng et al., 2022; U.S. EPA, 2009; Hohreiter and Rigg, 2001; U.S. EPA, 1987) and EPA-HQ-OPP-2007-0588-0140) but did not utilize the information due to the foregoing reasons. The Agency notes that a *Draft Proposed Approach for Consideration of Chemical Co-exposure in TSCA Risk Evaluations* peer-reviewed in 2024 (U.S. EPA, 2024b). In the consideration of chemical co-exposure, this document provides novel approaches and methods to evaluate chemicals that may co-occur with a specific chemical prioritized for risk evaluation, informing on chemical exposure and risk characterizations.

1.1.1.2 Comment

Summary: As a bulleted recommendation on page 39 of the SACC report, the SACC recommended that EPA should consider multiple sources of 1,3-butadiene releases to the environment, including automobile exhaust, tobacco smoke, wood burning, and industrial emissions, at least qualitatively if not quantitatively. They shared two references, Chen and Zhang, 2022 and Doyle et al., 2004, that highlighted the fact that automobile exhaust and tobacco are sources of 1,3-butadiene in the environment as well as the toxic effects of the degradation products of 1,3-butadiene.

EPA Response: EPA has reviewed both references. These references do not present novel information concerning environmental releases of 1,3-butadiene. EPA did not use these references (Chen and Zhang, 2022 and Doyle et al., 2004) because they did not provide any original data relevant to our specific evaluation needs. While they highlight important information about sources and effects of 1,3-butadiene, our focus was on original data that could directly inform our assessment criteria. However, EPA did qualitatively consider and contextualize multiple sources of 1,3-butadiene, including automobile exhaust (onroad and nonroad mobile sources), residential wood burning, natural fires through the AirToxScreen discussion in Section 2.3.2.2 of the *General Population Exposure for 1,3-Butadiene* (U.S. EPA, 2025c).

1.1.1.3 Comment

Summary: The physical-chemical properties of 1,3-butadiene suggest that releases of 1,3-butadiene to surface water will volatilize rapidly, and available release data show that 1,3-butadiene is not intentionally released to water. As a bulleted recommendation on page 39 of the SACC report, the SACC noted that continuous discharge of 1,3-butadiene to surface water could lead to the buildup of 1,3-butadiene concentrations in the water resulting in continuous, long-term exposure to aquatic organisms.

EPA Response: Updates have been made to Section 3.4.4 of the *Physical Chemistry, Fate, and Transport Assessment for 1,3-Butadiene* (U.S. EPA, 2025f) to clarify the possibility of exposure to aquatic organisms in the event of continuous releases of 1,3-butadiene to surface water. However, releases to water are low (based on data from TRI and DMR) and volatility is high, thus there is a low expectation of 1,3-butadiene presence in aquatic systems. See Section 2 of the *Physical Chemistry, Fate, and Transport Assessment for 1,3-Butadiene* (U.S. EPA, 2025f) for details on physical and chemical properties of 1,3-butadiene, *Water Releases for 1,3-Butadiene* (U.S. EPA, 2025q) for more details on releases to water and Section 4 of the *Environmental Media Concentrations for 1,3-Butadiene* (U.S. EPA, 2025b) for details on measured concentrations of 1,3-butadiene in water.

1.1.1.4 Comment

Summary: As a bulleted recommendation on page 39 of the SACC report, the SACC recommended including a map of the locations of facilities reporting 1,3-butadiene releases in the TRI and NEI databases and of injection wells, overlaid with locations of surface and groundwater sampling to give information on the geospatial relationship between monitored wells and potential injection wells or industrial facilities.

EPA Response: EPA did not develop the recommended map; as measured data for surface and groundwater were all below the detection limit for 1,3-butadiene in the Water Quality Portal (WQP) (U.S. EPA, 2025j). Based on its physico-chemical properties (High vapor pressure, high volatility and low solubility), national release data (TRI, DMR), and monitoring data (WQP), 1,3-butadiene is not expected or known to be present in surface or groundwater. Further, injection wells are designed and constructed to prevent the movement of injected waste streams into drinking water systems, as described in Section 3.4.5 of *Physical Chemistry, Fate, and Transport Assessment for 1,3-Butadiene* (U.S. EPA, 2025f). Hence, it is unlikely that this disposal pathway could contaminate a drinking water source. For details on the detection limits for 1,3-butadiene in the WQP, see *Water Quality Portal (WQP) Monitoring Data 2004 to 2025 for 1,3-Butadiene* (U.S. EPA, 2025j).

1.1.1.5 Comment

Summary: As a bulleted recommendation on page 39 of the SACC report, the SACC recommended omitting measured surface and groundwater data from states that have no 1,3-butadiene facilities and including states that do (*e.g.*, Louisiana). This would bolster EPA's conclusion that there is no unreasonable risk to aquatic ecosystems due to absence of reported environmental concentrations of 1,3-butadiene in surface and groundwater.

EPA Response: As one SACC panelist discussed, the locations of 1,3-butadiene facilities are widespread across the U.S., suggesting that the presence and potential impact of 1,3-butadiene could be significant even in areas without specific facilities, thereby warranting the inclusion of all measured surface and groundwater data in the assessment (see slide at EPA-HQ-OPPT-2024-0425-0102). Thus, EPA disagrees with the suggestion that states without facilities manufacturing or using 1,3-butadiene should be removed from the groundwater and surface water assessment. EPA has included a sentence in Section 6.2 of the *Environmental Media Concentrations for 1,3-Butadiene* (U.S. EPA, 2025b), acknowledging that some of the measured values may be from states with no 1,3-butadiene facilities. On the other hand, states where 1,3-butadiene facilities are located (including Louisiana) are included in the Water Quality Portal (WQP), which was an information source for the water assessment in the 1,3-butadiene risk evaluation.

Overall, 1,3-butadiene is not expected or known to be present in surface water or groundwater. Lines of evidence to support this conclusion include: 1) the fraction released to water from facilities (< 0.1%

[national] and <0.3% [Louisiana] reported in TRI) as described in *Water Releases for 1,3-Butadiene* (U.S. EPA, 2025q), 2) 1,3-butadiene's physico-chemical properties which make it volatile, not highly soluble in water, and not sorptive to soil or sediment as described in *Physical Chemistry, Fate, and Transport Assessment for 1,3-Butadiene* (U.S. EPA, 2025f), and 3) the absence of reported environmental concentrations of 1,3-butadiene as described in *Environmental Media Concentrations for 1,3-Butadiene* (U.S. EPA, 2025b). EPA employed all reasonably available data to conclude that water is not an exposure pathway for humans or aquatic ecosystems.

1.1.1.6 Comment

Summary: The SACC agreed that significant exposure to terrestrial organisms would not proceed through ingestion of or dermal exposure to water; however, the SACC disagreed that terrestrial organisms had limited atmospheric exposures and, as a bulleted recommendation on page 39 of the SACC report, recommended a quantitative screening assessment for mammals and a qualitative assessment for other classes of organisms.

EPA Response: Based on the SACC recommendation, EPA conducted a quantitative screen of the possible risk of 1,3-butadiene to terrestrial organisms via inhalation in ambient air using human health animal toxicity data and addressed qualitatively that sensitivities likely vary among taxa (see Sections 6.3.3 and 6.3.4 of the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g)). Specifically, the highest modeled and monitored concentration of 1,3-butadiene in ambient air are two orders of magnitude lower than the most sensitive ecotoxicity endpoint (non-apical effects at 20 ppm) for terrestrial vertebrate (mouse) inhalation (Brinkworth et al., 1998; Hackett et al., 1988; Thurmond et al., 1986); thus, potential risk to terrestrial organisms is not expected.

1.1.1.7 Comment

Summary: Although toxicity data are lacking for birds, the SACC recommended considering using data from bird species monitoring sources (Breeding Bird Survey, Audubon Christmas Count, Patuxent Research Refuge, etc.) to assess impacts to bird populations living near sources of 1,3-butadiene exposure as a bulleted recommendation on page 39 of the SACC report.

EPA Response: EPA did not use bird population monitoring data to assess risk to birds from exposure to 1,3-butadiene. The monitoring sources recommended by SACC monitor bird populations. These sources do not provide biomonitoring data related to chemical exposure (*e.g.*, tissue concentrations). 1,3-Butadiene exposure to wildlife, including birds, results from TSCA sources as well as non-TSCA sources. Potential changes in bird species population abundance or diversity near facilities that emit 1,3-butadiene identified from bird monitoring sources, if any occurred, could not be definitively attributed to exposure to 1,3-butadiene from TSCA sources as chemical concentrations in air are not collected in conjunction with bird population monitoring. The EPA does not have programs to monitor wild bird health and potential sources of exposure to chemicals.

1.1.1.8 Comment

Summary: As a bulleted recommendation on page 39 of the SACC report, the SACC recommended including descriptions of the uncertainties associated with the information used to assess environmental exposures and ecological risks.

EPA Response: EPA characterized confidence and uncertainties in the environmental exposure assessment and the environmental risk characterization in Sections 6.1.3 and 6.3.4, respectively, of the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g) including low environmental water releases and a high frequency of non-detects in the Water Quality Portal (WQP) monitoring data (U.S. EPA, 2025j);

and acknowledgement of known variation in sensitivities among taxa as highlighted by SACC in examples from Haider et al. 2021, Cape 2003, Tattersall 2007, Sanderfoot and Holloway 2017, Dumonceaux and Harrison 1994, Lackey et al. 1985, and Peng et al. 2022. There are no data evaluating toxicity of 1,3-butadiene to wildlife; thus, variable sensitivities to 1,3-butadiene among taxa are unknown.

1.1.1.9 Comment

Summary: As a bulleted recommendation on page 39 of the SACC report, the SACC noted that the 1,3-butadiene life cycle diagram, Figure 2-1 in Section 2.2 of the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g) incorrectly suggests 1,3-butadiene production and use form a closed system. They recommended updating the figure to include arrows to account for environmental releases from TSCA facilities and environmental fate.

EPA Response: EPA has included an arrow in Figure 2-1 in the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g) to account for environmental releases and fate. Previously, as the SACC noted, the diagram was set up as if 1,3-butadiene was not being released to the environment. Environmental fate is a consequence of environmental release so only one arrow is necessary to indicate release and subsequent fate.

1.1.1.10 Comment

Summary: As a bulleted recommendation on page 39 of the SACC report, the SACC noted that risk is inherently a probability of an adverse event and is always present to some extent. They noted that the critical consideration is whether risk is deemed acceptable or unacceptable and advise against viewing risk as a binary concept, and that instead that risk should be seen as a continuum. Terms like "reasonable" or "unreasonable" risk are preferred, as they reflect the non-absolute nature of risk. This perspective should inform responses to all related questions.

EPA Response: EPA has removed references to the term “no risk” throughout the final risk evaluation, replacing it with terms, such as, "reasonable," "unreasonable," or “negligible” risk, etc. consistent with statutory authorities.

1.1.1.11 Comment

Summary: The SACC supported the EPA's qualitative risk assessment approach for aquatic ecosystems and terrestrial organisms, concluding no significant risk from soil exposure or groundwater. However, SACC noted, on page 31, that ecological risks from potential spills during transport of 1,3-Butadiene, which is transported in liquid form, should be considered, and on page 31 of the SACC report, recommended that EPA evaluates how quickly the liquid would volatilize and its interaction with sediment or soil particles, as these factors could influence the risk to terrestrial and aquatic systems.

EPA Response: 1,3-Butadiene is a gas at atmospheric pressure and is only liquid under high pressures. In the event of a spill, 1,3-Butadiene would volatilize rapidly, reducing the risk to terrestrial and aquatic systems. 1,3-Butadiene will not readily adsorb to soil as described in *Physical Chemistry, Fate, and Transport Assessment for 1,3-Butadiene* (U.S. EPA, 2025f). EPI Suite™ estimated volatilization half-lives from water ranged from 0.76 hours in a model river to 2.9 days in a model lake. These volatilization half-lives are based on a depth of 1 m, wind velocity of 5 m/s and current velocity of 1 m/s for the model river and a depth of 1 m, wind velocity of 0.5 m/s and current velocity of 0.05 m/s for the model lake (See Section 3.4.4 of the *Physical Chemistry, Fate, and Transport Assessment for 1,3-Butadiene* (U.S. EPA, 2025f)). It is important to note that volatilization rates will depend on actual

conditions environmental conditions and water depth. Releases to water through spills are likely to occur to surface water where volatilization will be rapid. While spills may present an acute exposure to the environment, our assessment indicates low confidence for Points of Departure (PODs) associated with acute exposures and the POD for repeated exposures is expected to be protective of any potential acute hazard. Further, monitoring data have shown no measured concentrations of 1,3-butadiene in surface or groundwater. See Section 3.7 of the *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* (U.S. EPA, 2025p) for full text on spills, leaks, and accidents.

1.1.2 Charge Question 1a.ii

1.1.2.1 Comment

Summary: As a bulleted recommendation on page 40, the SACC suggested evaluation of environmental concentrations of transformation products (*e.g.,* acrolein and formaldehyde) to determine if a quantitative risk assessment is warranted.

EPA Response: See response to Comment 1.1.1.1.

1.1.2.2 Comment

Summary: As a bulleted recommendation on page 40 of the SACC report, the SACC suggested considering spills and/or unexpected releases of 1,3-butadiene in surface water.

EPA Response: As discussed in the scope for the 1,3-butadiene and other chemical scope documents, accidental releases, spills and severe weather have been considered out of scope for the TSCA risk evaluations. See also 87 Fed. Reg. 37028, 37033 (May 3, 2024) (distinguishing "regular or predictable" events from "those that are unsubstantiated, speculative or otherwise not likely to occur"). However, EPA has included a discussion on 1,3-butadiene activities under the Distribution in Commerce condition of use (COU), which includes some data on spills and releases of 1,3-butadiene in the *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* technical support document (U.S. EPA, 2025p). 1,3-Butadiene is a gas at atmospheric pressure and is only liquid under high pressures. In the event of a spill, 1,3-butadiene would volatilize rapidly. The likely volatilization of 1,3-butadiene is supported by water monitoring data which shows no measured concentrations of 1,3-butadiene in surface or groundwater. See response to Comment 1.1.1.11.

1.1.2.3 Comment

Summary: As a bulleted recommendation on page 40 of the SACC report, the SACC suggested acknowledging uncertainties in the surface water monitoring data set and expanding the data set to include more recent information if possible.

EPA Response: Discussion of monitoring data is detailed in Section 3.1.2 of the *Environmental Media Concentrations for 1,3-Butadiene* technical support document (U.S. EPA, 2025b). EPA also updated the information from the WQP database with recent monitoring. No additional surface water results were available. All of the samples were below the limit of detection for 1,3-butadiene. The measured water data and associated uncertainties and/or limitations are contained in Sections 4 and 6 respectively, of the *Environmental Media Concentrations for 1,3-Butadiene* (U.S. EPA, 2025b) which were updated to include more discussion of the limitations.

1.1.2.4 Comment

Summary: As a bulleted recommendation on page 40 of the SACC report, the SACC suggested mapping the locations of surface water sampling and industrial production/uses of 1,3-butadiene.

EPA Response: See response to Comment 1.1.1.4.

1.2 Charge Question 2 - General Population Exposure

1.2.1 Charge Question 2a.i

1.2.1.1 Comment

Summary: On page 42 of the SACC report, some Committee members agreed that the IIOAC modeling of ambient air concentrations to inform the non-cancer risk evaluation was appropriate, but some did not agree because of the model's limitations of not considering aggregate exposures, exposures to other chemicals (*e.g.* formaldehyde and acrolein), and PESS.

EPA Response: EPA acknowledges the limitations of IIOAC in its inability to aggregate emissions from multiple facilities in the same geographical area. As such, EPA conducted refined analyses with the HEM model, which included refinements in facility release input parameters, meteorological data and modeled concentrations at a greater range of distances (from 10 to 50,000 m) and aggregate Census block risk estimates from multiple facilities based on facilities' latitude and longitude coordinates.

1.2.2 Charge Question 2a.ii

1.2.2.1 Comment

Summary: As a bulleted recommendation on page 44 of the SACC report, the SACC asked EPA to clarify how aggregate exposures from multiple facilities were addressed in the HEM model and, on page 48, to continue using the Census block approach at greater distances and aggregating exposures from multiple 1,3-butadiene sources. The SACC highlighted several strengths and limitations of the HEM model. As a strength, they noted that the model has an easily understandable methodology, which enhances transparency. Additionally, it can provide results for all modeled facilities as a group and utilizes more meteorological data. However, they also pointed out certain limitations: the model's inability to identify PESS, its failure to account for exposure from releases of other sources, such as co-occurring chemicals and transformation products and TRI being the basis of both the HEM and IIOAC modeling.

EPA Response: EPA conducted refined analyses with the HEM model due to its ability to incorporate aggregate exposures and risks at the Census blocks level for up to 50,000 m away from facility releases (the maximum distance that can be modeled within HEM). EPA also acknowledges the use of TRI data and its limitations as a basis for both IIOAC and HEM modeling. Therefore, for the final risk evaluation, EPA further refined HEM modeling with NEI release data, which includes emission unit-specific release parameters, in the Section 5.3.4.3 of the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g).

1.2.2.2 Comment

Summary: As a bulleted recommendation on page 44 of the SACC report, the SACC recommended to overlay the locations of the points of release on Figure 5-1 of the 1,3-Butadiene Draft Risk Evaluation (U.S. EPA, 2024g).

EPA Response: In Section 5.3.4.3.2 of the final *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g), the US Census block figures have been revised to indicate locations of NEI facility releases.

1.2.2.3 Comment

Summary: As a bulleted recommendation on page 44 of the SACC report, the SACC requested EPA to review the spreadsheets from item 3D in the Environmental Defense Fund (EDF) comment (EPA-HQ-OPPT-2024-0425-0079). In the draft HEM NEI 2017 and 2020 Prelim Exposure and Risk Analysis spreadsheet, EPA appears to have switched columns G and H (stack height and exit gas temperature).

EPA Response: EPA has corrected the error in the switched columns G and H (stack height and exit gas temperature) in the final supplemental file HEM NEI 2017 and 2020 Prelim Exposure and Risk Analysis and has remodeled the NEI data accordingly with HEM.

1.2.2.4 Comment

Summary: As a bulleted recommendation on page 45 of the SACC report, the SACC recommended to use HEM's full range of radial distances in order to estimate human and environmental exposures.

EPA Response: In response to the SACC recommendation, EPA conducted refined analyses with the HEM model for the final risk evaluation due to the model's ability to make estimates for a larger range of radial distances and its ability to aggregate emissions from multiple facilities in the same geographical area in Section 2.2.3 of the *General Population Exposure for 1,3-Butadiene* (U.S. EPA, 2025c) and in Sections 5.3.4.2 and 5.3.4.3 of the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g). The full range of HEM radial distances is 10 m to 50,000 m. EPA used this full range to estimate human and environmental exposures.

1.2.2.5 Comment

Summary: The SACC noted on page 45 of their report that basing exposure and risk estimates on Census blocks from HEM model assumes that people live in one Census block for their entire lifetime. There is uncertainty in that assumption because people may move throughout their lifetime, which affects exposure duration.

EPA Response: EPA acknowledges the uncertainty in the assumption that people live in one Census block for their entire lifetime. However, this assumption allows for conservative exposure and risk estimates because EPA assumes that exposure is occurring over an entire lifetime rather than just residency time. Chapter 16: Activity Factors of the EPA Exposure Factors Handbook Section 16.5.2.2 reported on survey of 15,000 home buyers that when residents relocated, the distances moved to their new homes were typically short distances with about half of the of respondents (49%) relocating less than 5 miles to 9 miles from their old residence and 17% relocating more than 100 miles away. Therefore, although the assumption is conservative, the data suggest that it is plausible that some residents may relocate within the same census block, which vary greatly in size (from less than an acre to thousands of acres) and can change between each Census update. Nevertheless, EPA realizes that the assumption that residents never leave the Census block and are exposed 24 hours each day for a full lifetime is a conservative assumption.

1.2.2.6 Comment

Summary: The SACC noted on page 45 of their report that radial distances are not based on actual residential locations and can include parts of a facility which would be considered on-site.

EPA Response: EPA acknowledges that radial distances may not represent actual residential locations. As such, results based on Census blocks from HEM modeling, which are more representative of actual residential locations, are provided and discussed in Section 5.3.4 of the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g).

1.2.2.7 Comment

Summary: The SACC noted on page 45 of their report that Census data from 2020 were used in this analysis. Post-enumeration surveys from the 1990, 2000, 2010, and 2020 censuses found that certain groups are persistently undercounted (United States Census Bureau Post-enumeration surveys. 2024), including Black or African Americans, Hispanic or Latinos, and young children ages 0─4. These limitations of undercounting in the census were not addressed by the EPA in the 1,3-Butadiene Draft Risk Evaluation (U.S. EPA, 2024g).

EPA Response: EPA acknowledges that post-enumeration surveys find that certain groups may be undercounted in the U.S. Census data and added wording to reflect that in Section 5.3.7.3 of the final *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g). However, the U.S. Census data are the best data available to EPA to characterize exposure and risk estimates with respect to sociodemographic groups.

1.2.2.8 Comment

Summary: As a bulleted recommendation on page 48 of the SACC report, the SACC recommended updating the general population risk assessment to include aggregated 1,3-butadiene exposures from geographically clustered facilities and other 1,3-butadiene exposures. The SACC also recommended that EPA update the general population noncancer risk assessment to include cumulative risk of exposure to 1,3-butadiene and its transformation products.

EPA Response: EPA did include aggregate 1,3-butadiene exposures and cancer risk estimates from multiple facilities within 50,000 m through the HEM modeling. In response to SACC, EPA added aggregate exposure and noncancer risk estimates in Section 2.2.1.2.1 of the *General Population Exposure for 1,3-Butadiene* (U.S. EPA, 2025c). However, the impact of other chemicals, including transformation products, was not assessed in the risk evaluation for 1,3-butadiene. Data evaluated by EPA suggest that localized formation of the major transformation products from 1,3-butadiene, formaldehyde and acrolein, would not lead to a sustained or measurable increase in ambient concentrations beyond existing background levels. Therefore, secondary formation of formaldehyde and acrolein is not anticipated to significantly impact exposure or alter risk conclusions and these transformation products were not included in the risk assessment. There are three major reasons for this. Firstly, formaldehyde and acrolein are not uniquely attributable to 1,3-butadiene, as emissions from TSCA-regulated sources and other natural and anthropogenic activities, such as vehicle exhaust and secondary formation from other VOCs, far exceed the quantities that could reasonably be formed through atmospheric degradation of 1,3-butadiene released form TSCA facilities. Consequently, any incremental contributions from 1,3-butadiene photodegradation would be negligible relative to environmental releases and background levels of formaldehyde (U.S. EPA, 2024a), rendering formaldehyde as a 1,3-butadiene degradate immaterial to the risk characterization. Second, the atmospheric photodegradation of 1,3-butadiene involves complex radical-mediated pathways that are influenced by local photochemical conditions, including ambient concentrations of relevant radicals, sunlight intensity, temperature, and the presence of co-pollutants (Khaled et al., 2019; Vimal, 2008; Andersson and Ljungström, 1989). Any model-based estimation would entail considerable uncertainty and offer limited value for risk assessment purposes. Third, both formaldehyde and acrolein undergo rapid photodegradation in the atmosphere, with half-lives typically measured in hours. Due to this rapid degradation, these compounds do not persist or accumulate in the environment.

1.2.2.9 Comment

Summary: As a bulleted recommendation on page 48, the SACC recommended that EPA work with states and other monitoring network sponsors to ensure monitoring data and monitor locations are correctly reflected in this assessment.

EPA Response: In response to the SACC recommendation, EPA accessed the AMTIC database in April 2025 and validated the 2016 to 2022 data used in the 1,3-butadiene risk evaluation included monitoring data from state monitoring networks, *e.g.*, Texas Commission Environmental Quality (TCEQ) and Louisiana Department of Environmental Quality (LDEQ). In addition, EPA also conducted an evaluation of the Houston Regional Monitoring network (HRM) and the Shell Norco monitoring network, which were presented through SACC and public comments. Discussion of monitoring data is detailed in Section 3.1.2 of the *Environmental Media Concentrations for 1,3-Butadiene* technical support document (U.S. EPA, 2025b). EPA did not work directly with state monitoring and other monitoring network sponsors, but instead, incorporated updated and best available monitoring data that was available or made available to EPA for the final risk evaluation.

1.2.2.10 Comment

Summary: As a bulleted recommendation on page 48, the SACC recommended adding a table that identifies data used in the general population exposure assessment and an analysis with an indication of whether these data would likely over-estimate or under-estimate the exposure estimate. Such a table will help the reader to understand the degree of uncertainty in the fenceline exposure assessment.

EPA Response: EPA did not include a table to indicate whether data used in the general population exposure assessment would likely over-estimate or under-estimate the assessment. Instead, EPA detailed the release data that were used as inputs into the IIOAC and HEM modeling (TRI and NEI release) in the appendices of the *General Population Exposure for 1,3-Butadiene* (U.S. EPA, 2025c) and the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g), the methodology of the modeling approach and the modeling results and how those results were utilized. EPA also assumes that general population exposure is occurring continuously for 24 hours day, 365 days a year over a lifetime. The weight of scientific evidence and uncertainties with environmental release data are discussed in Section 6 of the *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* technical support document (U.S. EPA, 2025p) and the weight of scientific evidence for the IIOAC and HEM models, along with general population exposure parameters is discussed in Section 3 of the *General Population Exposure for 1,3-Butadiene* (U.S. EPA, 2025c) technical support document.

1.2.2.11 Comment

Summary: As a bulleted recommendation on page 48 of the SACC report, the SACC recommended EPA to provide more information describing how the assessment included parameters to protect PESS.

EPA Response: In response to the SACC recommendation, EPA added an aggregate non-cancer analysis in Section 5.3.4.2.1 of the final *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g) for PESS, specifically, communities/populations living within close proximity (within 5 km) to multiple facilities, using a previously peer-reviewed methodology from the Final Risk Evaluation for 1,4-Dioxane. In addition, discussion on cancer risk estimates based on sociodemographic information from the HEM modeling for populations living within 5 km of NEI facilities was updated and added in Section 5.3.5 of the final *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g). In addition, EPA assumed that the general population, including PESS, is exposed 24 hours a day, 365 days a year over a lifetime to modeled ambient air concentrations. This assumption leads to a conservative exposure scenario that is health protective.

1.2.2.12 Comment

Summary: As a bulleted recommendation on page 48 of the SACC report, the SACC recommended that EPA compare monitoring data to HEM output to ensure that HEM is not underpredicting 1,3-butadiene concentrations. The SACC suggested that if HEM is underrepresenting airborne 1,3-butadiene, the Agency could use the difference to develop an adjustment factor to increase exposure estimates at the respective radial distances.

EPA Response: In response to the SACC recommendation, EPA compared HEM modeling results to AMTIC monitoring results and determined that modeling and monitoring data, overall, are within similar ranges and orders of magnitude. Based on the histograms of monitoring data, the vast majority (~95%) of 24-hour and 1-hour monitored concentrations are below 1 µg/m^3. Therefore, EPA does not find that modeled concentrations are underrepresenting ambient air concentrations of 1,3-butadiene from facility releases and therefore an adjustment factor is not appropriate. Comparison between HEM modeling and monitoring is discussed in Section 2.3.1.1 of the *General Population Exposure for 1,3-Butadiene* technical support document (U.S. EPA, 2025c).

1.2.3 Charge Question 2a.iii

1.2.3.1 Comment

Summary: As a bulleted recommendation on page 51 of the SACC report, the SACC recommended utilizing both fenceline and emission monitoring (not modeling) data for exposure assessments.

EPA Response: EPA agrees with SACC's recommendation to use both fenceline and emission monitoring data in the exposure assessment and includes discussion of both fenceline monitoring data (obtained from OAR) and AMTIC Archive monitoring data in both the draft and the risk evaluation to contextualize modeled concentrations of 1,3-butadiene in the ambient air. However, in this situation, EPA disagrees with the recommendation to not utilize modeling data for exposure assessments. As discussed in the draft and revised risk evaluations, fenceline monitoring data are obtained on facility property and is not representative of concentrations of 1,3-butadiene in the general population where individuals live or frequent. This may be attributed to dilution of emissions in ambient air and whether nearby communities are located downwind of the facility. AMTIC monitoring data, while it may be representative of concentrations where individuals live or frequent, is a snapshot in time of 1,3-butadiene concentrations due to all contributing sources and cannot be attributed to a single COU. Modeling data, on the other hand: can be attributed directly to a COU; is based on a continuous release of 1,3-butadiene from the facility; estimates concentrations of 1,3-butadiene at multiple radial distances (and Census blocks) where people live or frequent; and thus, represents ongoing exposure due to industrial releases of 1,3-butadiene to the ambient air under COUs. Therefore, EPA finds utilizing modeled concentrations from multiple previously peer reviewed models represents best available science to estimate exposures and associated risk estimates under COUs. The strength of using the modeled concentrations to derive risk estimates is supported through EPA's use of fenceline and AMTIC monitoring data to contextualize the representativeness of modeled exposures use to derive risk estimates, risk determinations, and regulatory decision-making.

1.2.3.2 Comment

Summary: The SACC noted on page 47 of their report that facility sources are based on TRI information which is uncertain. They recommend facility locations should be reviewed by EPA to ensure they are correct. They note that flaring of industrial gases or fumes is not considered in TRI in all

cases and should be discussed in the document. They also note that default input parameters (like stack height of 10 meters) may not reflect actual facility parameters.

As a bulleted recommendation, the SACC recommended EPA to discuss TRI information and its limitations as the basis for the IIOAC and HEM modeling approaches.

EPA Response: EPA added additional narrative around the uncertainties with the TRI dataset in the revised General Population TSD (Section 3), including uncertainty with both TRI and NEI reported latitude/longitudes by industry and the potential impact of shifts in the actual locations based on visual inspection of maps using satellite imagery. EPA also included discussion around the stack parameters and uncertainties around those inputs in the draft TSD and retained that discussion in the revised TSD.

1.2.3.3 Comment

Summary: As a bulleted recommendation on page 51 of the SACC report, the SACC recommended that when TRI data are used for emission estimates, EPA should include ½ the reporting limit as an estimate for each non-reporting facility that uses 1,3-butadiene and suggested that a Maximum Likelihood Estimate (MLE) or censored regression (*e.g.*, Tobit regression) could be preferred to insertion of the same value for each facility.

EPA Response: In the final *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g) EPA evaluated both TRI and NEI release data. The NEI release data included many of these low-emitting facilities not required to report to TRI. This combined approach represents best available science for TSCA RE purposes.

1.2.3.4 Comment

Summary: The SACC, on page 50 of their report, referenced epidemiological studies by Matanoski and Schwartz (1987), Santos-Burgoa et al. (1997), and Delzell et al. (1996) that identified processes in styrene-butadiene rubber (SBR) production with higher potential exposures, including two processes omitted in the tables: utilities and pilot plants. Both can have higher releases. Utilities integrate a mixture of support operational processes that include much of the transfers of monomers and other products whose maintenance might offer opportunities for releases to the environment and workers' exposures. Pilot plants' "flexibility" and constant changes for the development of specialty products (*i.e.*, specialty rubbers) might increase the opportunity for exposures. It is unclear if the latter are considered in the table when referring to specialty rubbers.

Response: The studies pointed out in the comments were considered in EPA's systematic review but the summary data present in them was not utilized for the plastic and rubber polymerization OES due to the age of the datasets in the studies (the exposure estimates took place before the permissible exposure limit (PEL) was lowered from 1,000ppm to 1ppm). More recent studies that received high or medium quality score ratings were found during systematic review and used in the risk evaluation instead. In Delzell et al. (1996), the only of the three studies to provide medians for the datasets, the medians were between 0.7ppm and 1.7ppm for the six plants evaluated, which is between the same order of magnitude, or one order of magnitude above, the risk evaluation's central tendency exposure estimate of 0.4ppm. Delzell et al. (1996) and Santos-Burgoa et al. (1997) both included maximum concentrations, which were 64ppm and 374ppm respectively. These are within the same order of magnitude, or one order of magnitude above, the risk evaluation's high-end exposure estimates of 16.9ppm. The Matanoski and Schwartz (1987) file did not provide summary statistics. While it does not appear that data from pilot plants are specifically included within the risk evaluation, some of the datapoints included in the Plastics and rubber polymerization OES included worker exposure in utility areas.

1.2.4 Charge Question 2a.iv

1.2.4.1 Comment

Summary: As a bulleted recommendation on page 55 of the SACC report, the SACC recommended EPA to verify the modeled ambient air concentrations with measured concentrations from air monitoring networks.

EPA Response: In response to the SACC recommendation, EPA added comparisons between modeled concentrations using TRI and NEI release data with AMTIC 24-hour and 1-hour monitoring data in Section 2.3.1.1 of the *General Population Exposure for 1,3-Butadiene* technical support document (U.S. EPA, 2025c).

1.2.4.2 Comment

Summary: As a bulleted recommendation on page 55 of the SACC report, the SACC recommended that EPA evaluate industry compliance with TRI reporting and, at a minimum, describe that compliance in this assessment. It could also be possible to use the extent of industry non-compliance to develop adjustment factors that could be used to adjust the TRI data upward. Violation records of 1,3-butadiene releasing facilities and noncompliance should be evaluated by the EPA and that a statement regarding the number of non-reporting facilities should also be noted and compared to the number of reporting facilities to assist in the understanding of the potential for TRI to underestimate 1,3-butadiene quantities released.

EPA Response: EPA's use of 5-years of TRI reported release data (and refining where appropriate using multiple years of NEI reported release data) as direct inputs to the models is the best available science for evaluating general population exposures (and associated risks) for TSCA RE purposes. TRI includes all estimated and accidental releases for reporting facilities. EPA's previously peer reviewed methodologies applied in this 1,3-butadiene risk evaluation includes exposure scenarios with a series of conservative assumptions (including highest reported releases across multiple years of TRI reported releases, default stack parameters, fugitive area sources, distances very near facility release points, local meteorological data, lifetime exposures, and other factors) and integration of ambient monitoring data provides strength and confidence that EPA's assessment of 1,3-butadiene is health protective and is estimating risk based on the data.

The TRI Program is responsible for identifying facilities that are not in compliance with Section 313 of the Emergency Planning and Community Right-to-Know Act (EPCRA) and Section 6607 of the Pollution Prevention Act (PPA). Each year, the TRI Program contacts certain facilities as part of the TRI data quality process. TRI uses a variety of methods to identify non-compliance including identifying facilities that are reporting to other EPA/non-EPA programs but not to the TRI Program. EPA did not consider non-compliance and develop adjustment factors to adjust the TRI release data upwards because TRI already has quality controls surrounding their data quality. Please see this webpage on data quality https://www.epa.gov/toxics-release-inventory-tri-program/tri-data-quality-process (accessed December 10, 2025).

1.2.4.3 Comment

Summary: As a bulleted recommendation on page 55 of the SACC report, the SACC recommended EPA update both the non-cancer and cancer risk assessment for the general population by prioritizing use of monitoring data that represents true real-world exposures in the general population.

EPA Response: EPA disagrees with the recommendation to utilize monitoring data to update the non-cancer and cancer risk assessments for the general population. As discussed in the draft and revised risk evaluations, fenceline monitoring data are obtained on facility property and is not representative of concentrations of 1,3-butadiene in the general population where individuals live or frequent (general population does not live on facility property). AMTIC monitoring data, while it may be representative of concentrations where individuals live or frequent, is a snapshot in time of 1,3-butadiene concentrations due to all contributing sources and cannot be attributed to a single COU. Modeling data, on the other hand, can be attributed directly to a COU, is based on a continuous release of 1,3-butadiene from the facility, estimates concentrations of 1,3-butadiene at multiple radial distances (and Census blocks) where people live or frequent, and thus represents ongoing exposure due to industrial releases of 1,3-butadiene to the ambient air under COUs which occurs on an ongoing basis/continuous exposure. Therefore, EPA is utilizing modeled concentrations from multiple previously peer reviewed models to represent best available science to estimate exposures and associated risk estimates under COUs. However, fenceline and AMTIC monitoring data are discussed to provide context on general population exposures in the *Environmental Media Concentrations for 1,3-Butadiene* (U.S. EPA, 2025b) and the *General Population Exposure for 1,3-Butadiene* (U.S. EPA, 2025c) TSDs and to help support the use of modeled concentrations for non-cancer and cancer risk estimates. Overall, modeled concentrations from HEM based on both TRI and NEI releases are within the range and orders of magnitude with AMTIC monitoring concentrations.

1.2.5 Other Comments on Charge Question 2

1.2.5.1 Comment

Summary: The SACC noted on page 42 of their report that the person's [population's] habits and activity patterns, *e.g.*, time spent indoors or outdoors, time spent at home, at work or away from residence, etc. and biological variability, *e.g.*, susceptibility differences in male and female adults, children, elderly, pregnant women, varying body weights and inhalation rates, genetics, race, etc., were not considered in the IIOAC or HEM modeling for general population exposure.

EPA Response: EPA modeling with IIOAC or HEM did not take into consideration personal habits, *e.g.*, time spent outdoor vs. indoor, but assumed that the general population is exposed 24 hours a day, 365 days a year over a lifetime to modeled ambient air concentrations. This assumption leads to a conservative exposure scenario that is health protective. Biological variability, and susceptibility, and other factors were taken into consideration with respect to the hazard values detailed in Section 5.2 of the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g) using uncertainty factors for human variability and an age dependent adjustment factor (ADAF).

1.2.5.2 Comment

Summary: The SACC noted on page 47 of their report that from the User's Guide for the IIOAC, it appears the meteorological data are from 2011─2015 and do not match with the TRI data from 2016─2021. The timeframe of meteorological data used should be discussed.

EPA Response: EPA already included language noting that the 2011-2015 timeframe of meteorological data, integral to the IIOAC and used in the pre-run AERMOD scenarios, is one of the general limitations of the model in Section 3.1 of the *Draft General Population Exposure for 1,3-Butadiene* (U.S. EPA, 2024d). However, as part of the tiered analysis approach for general population exposures, EPA refined modeled estimates with the HEM model, which uses 2019 meteorological data that is more temporally aligned with the TRI data.

1.2.5.3 Comment

Summary: The SACC noted on page 47 of their report that based on 1,3-butadiene's fate properties in air with regards to forming transformation products (formaldehyde and acrolein) through photooxidation, and potential long-range transport based on half-life estimates, atmospheric reactions should be considered in EPA's air modeling (IIOAC and HEM) for general population.

EPA Response: EPA provides additional narrative in the revised general population TSD addressing this recommendation. In general, EPA did not consider photooxidation, half-life, and long-range transport in EPA's air modeling using IIOAC and HEM when evaluating general population exposures to 1,3-butadiene in the TSCA risk evaluation because the AERMOD Gaussian plume dispersion model on which both IIOAC and HEM does not have the capability to take secondary air pollutant formation under consideration. Additionally, although photolysis of 1,3-butadiene can occur, its photolytic half-life is 4.5 hours. During this time frame, natural dispersion of a plume, even under light wind conditions, would carry the dispersed plume far beyond the modeled distances where the EPA has identified exposures or associated risks of concern (approximately 1000 to 2500 meters). In many instances, the plume would extend well beyond the modeling domain of 50 km. Therefore, exposures of concern at the evaluated distances would occur before 1,3-butadiene undergoes significant photolysis. Furthermore, EPA's assumption of continuous release of 1,3-butadiene every day and every year (when evaluating life-time exposures) results in continuous exposure to 1,3-butadiene independent of how much may undergo photolysis. In essence, a continuous supply of 1,3-butadiene to a given exposed group would replenish any 1,3-butadiene which underwent photolysis on a continuous basis.

1.2.5.4 Comment

Summary: The SACC noted on page 52 of their report that the modeled concentrations in the *Draft General Population Exposure for 1,3-Butadiene* (U.S. EPA, 2024d) likely underestimate true real-world exposures. The SACC referenced reports and peer reviewed papers found monitored concentrations tend to be higher than modeled concentrations, including the Technology Review for Fenceline Monitoring supporting the New Hazardous Organic NESHAP and Padilla et. al, 2024. The SACC also noted that there are facilities with ambient air monitors nearby and concentrations could be modeled to that distance and compared to measured concentrations. The SACC recommended that EPA use concentration differences from upwind and downwind of the facility to quantify an estimate of concentrations from other sources and use that data to provide a validation of the models. One of the SACC members also noted that peer reviewed papers could be used to validate, confirm, or increase trust in the data that were used as inputs for models or in model outcomes.

EPA Response: An evaluation of The Technology Review for Fenceline Monitoring supporting the New Hazardous Organic NESHAP monitoring report was added to Section 2.3.2.1 of the *General Population Exposure for 1,3-Butadiene* technical support document (U.S. EPA, 2025c). In addition, EPA reviewed Padilla et. al, 2024, in which, the study concluded that there is an overall trend across all 79 hazardous air pollutants (HAPs) that monitored concentrations tend to be higher than modeled concentrations. However, out of all 79 HAPs, 1,3-butadiene resulted in the lowest bias with a median monitored to modeled bias ratio of 1.3; along with a median of 80% of monitoring measurements across the 360 monitoring stations were non-detects and/or reported as below the MDL. The study also applied adjustment factors based on the bias ratios to adjust risk estimates for two facilities in Houston, TX and Baton Rouge, LA as case studies. In the case studies, the adjustment factor for 1,3-butadiene was 1.0, *i.e.*, no adjustment, because the median modeled concentration (0.21 µg/m^3) was higher than the median monitored concentration (0.15 µg/m^3). In response to SACC, EPA added a comparison between modeled concentrations with monitoring data from the AMTIC monitoring database in Section 2.3.1.1 of the *General Population Exposure for 1,3-Butadiene* (U.S. EPA, 2025c). In terms of upwind and

downwind concentrations, the HEM models at 16 receptors (spaced every 22.5 degrees) at each radial ring distance (from 10 to 50,000 meters); *i.e.*, the receptors around each radial ring that are upwind for the emission release point would have lower modeled concentrations than the receptors that are downwind. EPA presents both the 95th and 50th percentile modeled concentrations at every radial distance, in which, the 95th percentile modeled concentrations are orientated more downwind than the 50th percentile modeled concentrations.

EPA included discussion of peer-reviewed papers in Section 3.1 of the *Environmental Media Concentrations for 1,3-Butadiene* technical support document (U.S. EPA, 2025b) and presented the findings from these studies. Measured concentrations of 1,3-butadiene in ambient air were extracted from five U.S. studies published between 1999 and 2015 and reported sample measurements ranged from non-detect to 1.91 µg/m^3 (Bereznicki, et. al, (2012). The measured concentrations from these studies were not used to validate, confirm or increase trust in modeled concentrations from IIOAC or HEM because EPA does not find it reasonable to compare measured concentrations from studies to modeled concentrations because they are not directly comparable. Measured concentrations from these peer-reviewed studies report concentrations based on the samples collected, which vary between studies with respect to time, location, sample numbers, sample collection methods and analyses, etc., while modeled concentrations are annual-averaged hourly concentrations that based on annual releases of 1,3-butadiene from facilities that are located across the United States. However, as a point of reference, HEM 50th percentile modeled concentrations at the 100 to 1000 m distance were as high as 80 and 25.79 µg/m^3 based on TRI and NEI release data, respectively. Modeled concentrations were instead compared to monitoring concentrations from the nationwide AMTIC network in Section 2.3.1.1 of the *General Population Exposure for 1,3-Butadiene* technical support document (U.S. EPA, 2025c) to evaluate whether modeling concentrations and the nationwide ambient monitoring data were comparable.

1.2.5.5 Comment

Summary: Line 331 of the Draft General Population Exposure document describes the use of 2016─2021 TRI data. Several SACC members requested on page 47 of their report that the EPA provide a quantitative justification for this interval. The specific concern relates to inclusion of COVID years, wherein facilities may have operated at lower capacity differently, *i.e.*, production upsets under or over normal practices. Also, the recent annual trends of 1,3-butadiene concentrations between 2016 and 2024 should be noted, emphasizing recent trends for 1,3- butadiene concentrations in ambient air near the facilities included in the assessment, if available, to ensure that the model input can be expected to be stable in time going forward.

EPA Response: It is EPA's standard procedures to include the most recent 5 years of TRI data upon the start of the risk evaluation, which were the 2016 to 2021 TRI reporting years. A sixth year was included in the case of this evaluation due to the timing of the 2021 TRI release. In addition, although not used in the risk evaluation for 1,3-butadiene, EPA also queried more recent TRI reporting years: 2022 to 2024. The total stack and fugitive air releases per year are summarized in Table 1-1 below. In regard to the 2016 to 2021 reporting years, the total reported stack air releases were 8.8% lower, or over 30,000 kg less, in 2020 than the next lowest year (2018). Despite being lower than the other years, this amount of change is within the observed fluctuation range of total releases that occurred in previous years, for example there was a change of over 100,000 kg in total stack releases from 2018 to 2019. In the case of fugitive releases, the observed total releases in 2020 were not the lowest observed within the time range, with both 2017 and 2018 reporting lower total fugitive releases.

When comparing the 2022 to 2024 TRI reporting years to 2016 to 2021, the releases were similar.

Although the COVID pandemic may have impacted facility releases for this year, EPA has determined that the observed impact did not justify analyzing the releases any differently than other years.

Table 1-1. TRI Annual Stack and Fugitive Air Releases per Year

	2016	2017	2018	2019	2020	2021	2022	2023	2024
Stack (kg)	402,128	459,895	357,218	471,927	325,629	379,989	400,639	375,699	381,982
Fugitive (kg)	158,088	149,745	140,613	167,970	157,471	163,852	150,926	148,643	139,104

1.2.5.6 Comment

Summary: The SACC noted on page 42 of their report that all data were averaged (yearly averaged and daily averaged), using six years of TRI data; this averaging eliminates excursions from the average, including potential concentration peaks. These data also included COVID pandemic years, during which industrial production was lower than normal. Each of these factors lowers the predicted worst case or "high-end" exposures, thus minimizing the health protectiveness of the risk evaluation.

EPA Response: In response to the SACC, EPA added discussion around the assumptions associated with using annual release data from TRI (and NEI which is every 3-years) as well as continuous operation and the daily release values used as inputs to EPA's air dispersion models in Section 5.3.7.3 of the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g). While these assumptions may miss potential peak releases occurring outside of normal operation, such peak releases are more applicable to short-term, acute exposures for which EPA does not have an acute POD and did not assess for 1,3-butadiene. Additionally, while EPA did consider six years of TRI data, EPA modeled both individual years of data (thus capturing higher individual yearly reported releases) as well as the highest releases across all six years of TRI data evaluated in Section 5.4.3.2.3 of the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g), which minimizes the potential impact of COVID pandemic years.

Regarding the impact of the COVID pandemic years, Table 1-1 above shows the total stack and fugitive air releases from TRI for each of the 6 years assessed. In regard to the 2016 to 2021 reporting years, total reported stack air releases were 8.8% lower, or over 30,000 kg less, in 2020 than the next lowest year (2018). Despite being lower than the other years, this amount of change is within the observed fluctuation range of total releases that occurred in previous years, for example there was a change of over 100,000 kg in total stack releases from 2018 to 2019. In the case of fugitive, the observed total releases in 2020 were not the lowest observed within the time range, with both 2017 and 2018 reporting lower total fugitive releases.

When comparing the 2022 to 2024 TRI reporting years to 2016 to 2021, the releases were similar. Although the COVID pandemic may have impacted facility releases for this year, EPA has determined that the observed impact did not justify analyzing the releases any differently than other years.

1.2.5.7 Comment

Summary: The SACC noted on page 49 of their report that both TRI and NEI data are self-reported and are only estimates (*i.e.*, rarely ever do facilities quantitatively measure their emissions).

EPA Response: Both the TRI and NEI datasets include information which indicates the basis for deriving the reported releases. For TRI reporting, the owner or operator of a facility should use its best

readily available data when submitting information to EPA. When data are not readily available, the owner or operator may use 'reasonable estimates' of the amounts released. The TRI reporting standard and form require the inclusion of a basis of estimate code to describe how the associated release quantity was calculated (*i.e.*, continuous monitoring, periodic monitoring, mass balance calculations, emission factors, or other approaches such as engineering calculations). EPA recommends that the facility document the reasoning used to support what was reported and maintain records. EPA may request these records during an inspection.

1.2.5.8 Comment

Summary: The SACC noted on page 50 of their report that acute and intermediate exposures could occur during accidental releases resulting from equipment malfunction, operator errors, spills, and severe weather.

EPA Response: As described in the *Scope of the Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2020b), exposures resulting from accidents, spills, and other releases are outside the scope of the risk evaluation because they cannot be reliably predicted or reasonably foreseen. However, EPA has included a discussion on 1,3-butadiene activities under the Distribution in Commerce condition of use (COU), which includes the presentation of some data on spills and releases of 1,3-butadiene in the *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* technical support document (U.S. EPA, 2025p). 1,3-Butadiene is a gas at atmospheric pressure and is only liquid under high pressures. In the event of a spill, 1,3-butadiene would volatilize rapidly. The likely volatilization of 1,3-butadiene is supported by water monitoring data which shows no measured concentrations of 1,3-butadiene in surface or groundwater. See response to comments 1.1.1.11 and 3.7.11.

1.2.5.9 Comment

Summary: The SACC noted on page 51 of their report that continuous processing and assumptions of average release during the year, given that TRI is an annual reporting system, should be evaluated for the possibility that not all manufacturing facilities and not all processes yield continuous exposure; in several instances processes are batch. Most of the polymerization production plants are continuous, given safety and efficiency considerations, but some operate in batch mode. The above-mentioned two considerations are relevant given the statement by the EPA of a "preference to rely on facility-specific releases."

EPA Response: EPA's ambient air analysis does not consider average daily releases during the year when evaluating general population exposures since EPA has not identified and industry has not provided actual hourly or daily monitored releases of individual chemicals to be considered for TSCA risk evaluations which could be used to calculate an average daily release. Since such hourly or daily release data are not available, EPA considers reasonably available information including industry reported annual releases, industry reported operating days, other reasonably available information and assumes a continuous release across all days of operation to determine the daily average release value used as direct inputs to air models. This daily release estimate takes into account the quantity of releases due to both batch and continuous operations that may be occuring at the facility over the course of the year, but EPA does not consider releases specific to batch operations in its analysis and assumes continuous release for the purposes of the risk evaluation. EPA assumes that the release days are equal to the operating days at a facility.

1.2.5.10 Comment

Summary: The SACC noted on page 50 of the SACC report that the EPA describes that "NEI emissions data are categorized into (1) point source data, (2) area or nonpoint source data, (3) onroad

mobile source data, and (4) nonroad mobile source data. EPA included only point source data categories in the assessment of environmental releases in this risk evaluation." Therefore, the EPA has the requisite information to consider aggregate estimation, something that would better estimate the real impact of the additional exposure from industrial emissions. The *Draft Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* document (U.S. EPA, 2024h), indicates that "1,3-Butadiene is also generated as a byproduct from the incomplete combustion of fuel. EPA did not assess environmental releases or occupational exposures resulting from 1,3-butadiene formed as a byproduct (e.g., exhaust emissions). EPA believes it is more appropriate to evaluate the potential risks arising from the byproduct within the scope of the risk evaluation for fuel from which the 1,3-butadiene is produced, rather than the 1,3-butadiene risk evaluation." This rationale for not conducting a full aggregate assessment should be clearly justified. The current quote from the EPA also provides justification for including formaldehyde and acrolein risks in the 1,3-butadiene risk evaluation.

EPA Response: The NEI point source data includes both fugitive and stack release information from industrial facilities which can be attributed to a COU. The releases EPA cannot attribute to a COU identified by the commenter are evaluated by EPA's Office of Air and Radiation as part of the AirToxScreen process and EPA does present a summary of AirToxScreen results in the draft and final 1,3-butadiene risk evaluations to help contextualize other sources contributions to total ambient air concentrations of 1,3-butadiene. For discussion on why formaldehyde and acrolein risks are not considered in the 1,3-butadiene risk evaluation, refer to EPA's response to comment 1.1.1.1.

1.2.5.11 Comment

Summary: One SACC committee member, on page 51 of the SACC report, expressed concern with underground injection wells that are used to dispose of 1,3-butadiene but did not provide further recommendations. Given the lack of solar irradiation and the stability of the monomer, 1,3-butadiene could be present in injection wells for long periods. This source could be a potential concern in the future. This SACC member provided examples of the Del Amo facility in California, which was a former styrene monomer production, butadiene monomer production, and styrene butadiene plant that opened in 1943 and closed in 1971 and is now on the National Priorities List (NPL) along with another site at Fort Detrick, Maryland. Although 1,3-butadiene is not designated as a chemical of concern at these sites, 1,3-butadiene was identified in groundwater at Fort Detrick.

EPA Response: The Hazardous and Solid Waste Amendments (HSWA) to the Resource Conservation and Recovery Act (RCRA) added significant restrictions on the disposal of hazardous waste. Under these amendments, land disposal of hazardous wastes, which includes Class I hazardous waste injection wells, is prohibited unless the waste has been treated to become non-hazardous or the disposer can demonstrate that the waste will remain where it has been placed for as long as it remains hazardous, which has been defined as 10,000 years by regulation.

Potential pathways through which injected fluids can migrate to underground sources of drinking water include failure of the well, or improperly plugged or completed wells or other pathways near the well. Drinking water source contamination due to well failure is typically caused by leaks in the well tubing and casing or when injected fluid is forced upward between the well's outer casing and the well bore should the well lose mechanical integrity.

Well failures can be detected by continuous monitoring systems or mechanical integrity tests, at which point the wells would be shut-in until they are repaired. EPA's extensive technical requirements for UIC

Class I wells are designed to prevent contamination of underground sources of drinking water through these pathways.

Operators must conduct appropriate mechanical integrity tests yearly for hazardous wells and every 5 years for nonhazardous wells to ensure wells are fit for operation. It should be noted that the loss or failure of mechanical integrity does not necessarily mean that wastewater will escape the injection zone. This added security can be attributed to redundant safety systems to protect against loss of waste confinement. For more information on UIC Class I wells, see the UIC EPA website (accessed December 10, 2025) .

1.2.5.12 Comment

Summary: On page 38 of the SACC report, the SACC had the following concerns about the measured water samples presented in the 1,3-butadiene risk evaluation: There was a small and geographically limited sample of surface water measurements available, and the public water systems data did not include the number of samples or specify whether they were from groundwater or surface water.

EPA Response: For the draft RE, EPA included data sourced from the National Water Quality Portal (WQP) and the Third Unregulated Contaminant Monitoring (UCMR3). All the measured samples were below the detection limit for 1,3-butadiene. After the SACC meeting, EPA searched the NPDES data base for additional measured water samples. The NPDES database did not include monitoring data for 1,3-butadiene. EPA also went back to the WQP database in July 2025 and found recent monitoring samples for groundwater from 2024 and 2025, but all of the samples were below the limit of detection for 1,3-butadiene. The measured water data and associated uncertainties and/or limitations are contained in Sections 4 and 6 respectively, of the *Environmental Media Concentrations for 1,3-Butadiene* (U.S. EPA, 2025b). Section 4 has also been updated to include the number of drinking water samples. The UCMR3 data are available as a new supplemental document titled *Third Unregulated Contaminant Monitoring Rule Data for 1,3-butadiene* (U.S. EPA, 2025i). It clarifies which drinking water samples are sourced from surface water and which are sourced from groundwater.

1.3 Charge Question 3 - Consumer Exposure

1.3.1 Charge Question 3a

1.3.1.1 Comment

Summary: The SACC did not find the qualitative assessment for consumer exposures and risks sufficient and recommended that EPA conduct a quantitative analysis for 1,3-butadiene in consumer products. Specifically, as a bulleted recommendation on page 59 of the SACC report, the SACC recommended to replace “qualitative assessments” with Tier 1 quantitative assessments, explaining all assumptions and/or extrapolations about release rates, dermal exposures, air concentrations, etc. and to use very protective conservative assumptions for these exposure calculations when the EPA has not been given fundamental information about 1,3-butadiene residue in different plastic and rubber matrices or release rates of 1,3-butadiene under different environmental (temperature) or product use and degradation conditions.

EPA Response: In response to the SACC recommendation, EPA added a sensitivity analysis for consumer exposure and risks, using the Consumer Exposure Model (CEM) in Section 5.3.3 of the final *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g). EPA used CEM to model exposure and dose across a range of 1,3-butadiene weight fractions and surface areas of toys for infants along with exposure parameters from the EPA Exposure Factors Handbook (U.S. EPA, 2011). The weight fractions

evaluated ranged from a weight fraction of 0.001 (0.1%) to 0.3 (30%) and the surface area of the toy ranged from 1 m^2 to 4 m^2. This matrix of ranges, for both weight fraction and surface area, allows for conservative consumer exposure and risk estimates. Even under the assumption with a toy with a weight fraction of 0.3 (30%) and surface area of 4m^2, EPA did not find risk estimates that exceeded the benchmark. Notably, the highest amount of 1,3-butadiene reported from systematic review in toys was a weight fraction of 5.3×10^{-6} (0.00053%) (Abe et al., 2013, referenced by comment 0425-0118), which is almost three orders of magnitude below the inputs used in the model.

1.3.1.2 Comment

Summary: The SACC recommended on page 59 of the SACC report that EPA reword the explanation of risk to alter statements of "zero risk" to include terminology such as "minimal" or "exceedingly low" risk, consistent with the quantitative results of Tier 1 calculations and combined COUs where possible.

EPA Response: EPA has removed verbiage suggesting "no risk" in the final *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g) and replaced it with the term "minimal risk".

1.4 Charge Question 4 - Occupational Exposure

1.4.1 Charge Question 4a

1.4.1.1 Comment:

Summary: The SACC recommended on page 62 of the SACC report that the grouping of COUs should be based on the similarity of operations and exposures, and not on the availability of data. The SACC noted that there may be advantages for using American Industrial Hygiene Association methods to conduct similarly exposed group (SEG) determinations that take into consideration that the type and nature of exposures can vary within the same operation. The SACC also suggested that a tiered approach should be used to determine the best method for assessing exposure for each group, starting with screening-level assessments and increasing complexity as required in higher tiers.

EPA Response: Section 1.2 of the *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* (U.S. EPA, 2025p) describes EPA's method of determining the appropriate OESs for each COU. It is EPA's intention to group OESs based on similarity of operations and exposures, and to estimate relevant exposures as accurately as possible. However, the availability of data for each of these operations is a consideration, given that there is limited information on some tasks. Where possible, OESs are broken down into multiple activity-specific similarly exposed groups (SEGs). Otherwise, OESs will have two exposure estimates (one for workers, one for occupational non-users (ONUs)) when there was not enough information with which to estimate more granular exposures. EPA has reevaluated the OES mapping decisions in the risk evaluation as recommended, considering the SACC's recommendation to prioritize a similarity in operations and exposure potentials, rather than depending upon data availability, when making mapping decisions. In the final risk evaluation, EPA has separated out a new OES (Plastics and rubber polymerization) when it was found that exposures to this operation are unique to those found in Plastics and rubber compounding.

EPA acknowledges the suggestion to utilize a tiered approach to risk evaluation. A tiered approach was utilized in the OESs of Application of paints and coatings, and Application of adhesives and sealants. The monitoring data associated with these activities for which 1,3-butadiene was assumed to be present was entirely below the method limit of detection. EPA conservatively assessed risk at the LOD for high-end exposure and half the LOD for central tendency exposure. When no risk was found with these conservative assumptions, evaluation of additional tiers was not necessary. Similarly, there were cases

when high exposure was estimated for some OESs that used a task-based dataset (such as Repackaging, which had exposure estimates in the draft based on a task-based dataset that was assumed as-is to represent a full-shift of exposure). Assuming a task-based sample is representative of a full shift of exposure is a conservative assumption, and so if no risk calculations met the benchmark risk values, then no further assessment would have been completed. However, since risk was found, EPA has bolstered the assessment with a task-length assumption in the final document, with the assumption that the exposure only occurs for the duration of the task, with no exposure for the remaining 8 hours outside of the duration of the task. This assumption serves as a lower end estimate to better understand the range of possible exposures for the group. More information about this case can be found in Section 3.2 of the *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* (U.S. EPA, 2025p). The Waste handling, treatment, and disposal OES and the Recycling OES have been similarly updated with these assumptions using a tiered approach.

1.4.1.2 Comment

Summary: On page 63 of the SACC report, the SACC recommended that EPA refrain from considering any potential exposure reduction effects of PPE in exposure determinations and risk evaluations and instead should consider this information in risk management.

EPA Response: Although Table 5-5 in the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g) explores the reduction of exposure due to certain levels of PPE, EPA would like to clarify that it does not assume the use of PPE when estimating occupational exposure, as stated in the first paragraph of Section 2.4 of the *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* (U.S. EPA, 2025p).

1.4.1.3 Comment

Summary: On page 63 of the SACC report, the SACC recommended that EPA consider utilizing information on the controls in place (other than PPE), linked to workplace exposure measurements, in order to judge the effectiveness of those controls in reducing risk.

EPA Response: EPA was unable to quantify the effectiveness of non-PPE exposure controls but has added more information where available about exposure controls other than PPE relevant to each OES in Section 3 of the *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* (U.S. EPA, 2025p).

1.4.2 Charge Question 4ai

1.4.2.1 Comment

Summary: As a bulleted recommendation on page 64 of the SACC report, the SACC noted that the EPA's procedure for assessing non-detects is considered a substitution method and suggested using statistical methods instead due to the high number of non-detects within most of the datasets. Several alternative methods were suggested, such as maximum likelihood estimation, and censored regression techniques (*e.g.* Tobit regression. On page 71 of the SACC report, the SACC also recommended the use of the IH Data Analyst or a similar tool to facilitate the application of these estimation methods to the multiple data sets included in the 1,3-butadiene risk evaluation.

EPA response: EPA conducted an analysis of the occupational exposure datasets used in the risk evaluation and agreed with SACC's recommendation of using the maximum likelihood estimation and conducted that analysis for use in the risk evaluation. Section 2.4.3.1 of the *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* (U.S. EPA, 2025p) describes EPA's modified

method. In cases where a dataset had five or more uncensored datapoints, maximum likelihood estimation (MLE) assuming a lognormal distribution of concentrations was used to produce 50th and 95th percentiles to represent central tendency and high-end respectively. In cases where there were too few measured datapoints to perform more robust analysis such as MLE, EPA estimated the exposure concentrations for these data following EPA's Guidelines for Statistical Analysis of Occupational Exposure Data (EPA, 1994) which recommends using the LOD/√2 if the geometric standard deviation of the data is less than 3.0 and LOD/2 if the geometric standard deviation is 3.0 or greater and noted the uncertainty in the weight of scientific evidence (Section 5 of *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* (U.S. EPA, 2025p)).

EPA appreciates SACC's sharing of tools to assist in facilitating the assessment.

1.4.2.2 Comment

Summary: As another way to assess a dataset with a large number of non-detect samples, the SACC recommended on page 64 of the SACC report that EPA perform two separate exposure calculations, the first assuming exposure values at the LOD for non-detects, and the second a repeat of the calculation using zero for non-detects, in order to bracket exposure estimates and frame the uncertainty.

EPA response: EPA considered the options provided by SACC and determined that use of MLE was the best choice moving forward for datasets that had enough measured values with which to do the analysis.

1.4.2.3 Comment

Summary: The committee further commented on a point that it noted was not raised in the charge questions, but that the SACC considered deserving of attention. As bulleted recommendation on page 65 of the SACC report, the SACC suggested that EPA, in addition to its analysis assuming that no exposure occurred during shift time that was not measured, perform a separate analysis with the assumption that exposure during the unmeasured time was equal to the measured concentration, in order to create an "upper" possible 8-hr time-weighted-average (TWA) exposure estimate. It was suggested that this could serve as a sensitivity analysis, allowing the EPA to have a range of exposure for samples collected for less than the full shift.

EPA Response: For those OESs that utilized task-based sampling (Repackaging, Recycling, and Waste handling, Treatment, and Disposal), in the draft risk evaluation, the second assumption recommended by SACC was used; the assumption that the measured task-length exposure occurred through the entirety of the shift. In the final risk evaluation EPA included both of the recommended assumptions, adding the first recommended assessment that assumes the measured exposure occurs only for the stated duration of the task with no exposure for the remainder of the 8-hour shift. The final risk evaluation now shows the range of possible exposures based on the samples collected for less than a full shift, as suggested by SACC. Details can be found in Section 3 of the *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* (U.S. EPA, 2025p).

1.4.2.4 Comment

Summary: As bulleted recommendations on page 67 of the SACC report, the SACC recommended that EPA should explore the use of modeling as supplemental information for each OES lacking sufficient empirical data to provide a high confidence assessment, and there was a related recommendation to document the rationale for including or not including such modeling results to support the final exposure estimates. It was suggested that EPA consider the tire crumb study that examines possible exposure to residual 1,3-butadiene from tire crumbs and determine an "upper bound" or range of *de minimis*

residuals that do not require further assessment; it was suggested to evaluate the residuals using a modeling approach with defined sentinel scenarios. The SACC also noted that EPA could use modeling to obtain more confident estimates from left-censored data, particularly if statistical modeling cannot provide supportable results, and/or consider comparing that risk result with the risk result using near-field air modeling or other surrogate approaches to enhance the overall evidence for an exposure estimate.

EPA Response: In response to the recommendation and where possible, EPA utilized maximum likelihood estimation (MLE) to estimate the high end and central tendency exposures from highly left-censored datasets. Relevant to other modeling methods, the hierarchy of EPA's preferred approaches, presented in Section 2.4 of the *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* (U.S. EPA, 2025p), describes EPA's assessment preferences. The hierarchy indicates inhalation monitoring data as the highest preference. For OESs with few quantified datapoints (for example, Recycling and Waste handling, Treatment, and Disposal), EPA did not find available modeling methods that would have provided more robust results.

EPA has also clarified the information about 1,3-butadiene residuals in rubber used from the tire-crumb study and the applicability to the occupational risk evaluation in Section 3.14.1. To further support the lack of need for further assessment in finished plastic and rubber products, EPA added a sensitivity analysis, using the Consumer Exposure Model (CEM) in Section 5.3.3 of the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g).

1.4.2.5 Comment

Summary: As a bulleted recommendation on page 68 of the SACC report, the SACC has requested that EPA clarify the intended goal of the use of central tendency and high-end estimates and document the rationale for the approach to calculating each of these estimates relative to the specific end points used for each aspect of the risk determination. The comment expressed that for protecting all or nearly all workers from a chronic cumulative effect (like cancer) the high-end estimate of the actual mean is a metric to consider (*i.e.,* the 95% upper confident limit (UCL) of the mean), as opposed to the high-end of the daily exposure distribution. In the SACC's view, estimating the high-end of the exposure distribution would be more pertinent to ensuring that all or nearly all workers are protected from the potential for a single day of exposure to that daily TWA concentration which is most relevant to an acute daily limit (and possibly an intermediate duration limit depending on the mode of action). It was noted that the high-end values may be uncommon for a single individual worker to experience every day for a working lifetime, and not a good reflection of the high-end estimate of a daily average mean exposure.

EPA Response: The intended use of the central tendency and high-end estimates are described in Section 2.4 of the *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* (U.S. EPA, 2025p). In most cases, the central tendency and high-end are the 50th and 95th percentile of all exposure data respectively. It is uncommon for EPA to have enough data to determine a 95th upper confidence limit of the mean for an OES, and to use this in place of the 95th percentile of all exposures may underestimate shorter term risk such as acute and intermediate. EPA agrees that the high-end estimate based on monitoring data from as little as one workday is more appropriate for estimating shorter term exposures and associated risks, such as acute and intermediate. EPA's risk determination for 1,3-butadiene generally relies on high-end estimates to support its determination for workers for shorter term inhalation exposures (*i.e.,* intermediate non-cancer risk covering average exposures over one month) because consistent high-end exposures are more likely to occur over shorter time periods,

while central tendency estimates are used for longer term exposures (*i.e.*, several decades for chronic non-cancer and cancer).

1.4.2.6 Comment

Summary: As bulleted recommendations on page 72 of the SACC report, the SACC requested that EPA describes each COU and OES more completely where analogous data were used, as well as the OES or COU that was the source of the data used as analogous and provide the reasoning behind the choice. The SACC also recommended that EPA should also evaluate all OES groupings to confirm that each represents a similarly exposed group that can be evaluated with a single exposure assessment.

EPA Response: In response to the recommendation, EPA has expanded description of the monitoring data used in the assessment for each OES in Section 3 of the *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* (U.S. EPA, 2025p), including rationale for selection as the best option, the specific tasks that were measured while the sample was being collected, how the data were processed for use in the assessment (such as assumption for non-detects, and task-length samples) and how that task relates to the specific OES being assessed. In the risk characterization (Section 5.3.2 in the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g)) and weight of scientific evidence sections (Section 5 of the *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* (U.S. EPA, 2025p)), EPA includes discussion on the origin of the central tendency (CT) and high-end (HE) estimates, and if applicable explains if one estimate is more appropriate to use than the other.

The OESs that utilize analogous monitoring data (Repackaging, Incorporation into Formulation, Laboratory use, Recycling, and Waste handling, Treatment, and Disposal) have been more thoroughly discussed in the *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene*, see Sections 3.2.4, 3.4.4, 3.8.4, 3.12.4, and 3.13.4 (U.S. EPA, 2025p). This additional discussion provides a better understanding of the data that were used to estimate occupational risk in these cases, and why they were used despite not being directly applicable to the relevant OES. The applicability and limitations of these cases are more thoroughly discussed in the Weight of Scientific Evidence Conclusions, Section 6.2 of the *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* (U.S. EPA, 2025p). EPA considered the use of models or surrogate data (data from the same OES but for a different chemical) for these OESs, however EPA did not find models relevant to the needed exposure groups that were suitable for 1,3-butadiene, nor surrogates that matched the physical properties or uses of 1,3-butadiene in the relevant settings. More applicable monitoring data were also not found for these cases.

EPA has examined the other OES groupings and determined that 1,3-butadiene polymerization was not adequately examined within the draft risk evaluation, and so a new OES was designated for the final called Plastics and rubber polymerization. This OES used occupational exposure data found in systematic review for its exposure estimates.

1.4.3 Charge Question 4bi

1.4.3.1 Comment

Summary: As bulleted recommendations on page 77 of the SACC report, the SACC recommended that EPA include a screening-level or Tier 1 exposure assessment for occupational dermal exposure to 1,3-butadiene vapors, as opposed to the qualitative exposure assessment used in the draft. Such a screening-

level quantitative assessment could be performed and documented using a modeling tool such as IH SkinPerm. The SACC recommended adding a brief statement regarding a screening-level or Tier 1 assessment using physicochemical properties for occupational dermal exposure through liquids such as water or oils. The SACC also recommended considering the likely inclusiveness of vapor phase exposure potential by the dermal route in the potency estimate for the risk benchmarks. This expectation aligns with public information regarding handling guidelines. However, the EPA's document states, "EPA did not identify information on worker personal protective equipment (PPE) used at 1,3-butadiene manufacturing sites" (Lines 1566─1568 in (U.S. EPA, 2024b)). This is surprising as such information likely exists, and the EPA should try to verify this statement.

EPA Response: Section 2.4.5 was added to the *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* (U.S. EPA, 2025p), which describes in more detail 1,3-butadiene's characteristics in why dermal exposure is not expected in its liquid form or within a solution of water or oil. EPA also added a discussion on possible dermal exposure via vapor phase of 1,3-butadiene, citing Weschler and Nazaroff (Weschler and Nazaroff, 2014) which calculated that the transdermal permeability coefficient (k_{p_g}) of a compound must be greater than or equal to 0.025 m/hr for vapor to skin exposure to be considered relevant compared to inhalation exposure. Since 1,3-butadiene has a k_{p_g} of 5.02×10^{-5} m/hr, dermal exposure to vapor phase 1,3-butadiene is not considered a significant exposure pathway compared to inhalation and it is not considered further in this assessment.

Relevant to EPA's statement that PPE was not identified at 1,3-butadiene manufacturing sites, this statement was erroneous. EPA has added PPE information about the Manufacturing COU to Section 3.1.4.1 of the *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* (U.S. EPA, 2025p), which does specify the use of chemical protective gloves, suits, and boots for certain tasks handling 1,3-butadiene to prevent dermal contact.

1.5 Charge Question 5 – Human Health Hazard

1.5.1 Charge Question 5a.i

Summary: The SACC noted on page 79 of the SACC report that the EPA's preliminary determination not to derive an acute POD was understandable, given the complexity and limited data. However, the SACC suggested that the EPA consider alternative options, including potentially leveraging: (1) the interim AEGL-1 (Acute Exposure Guideline Level 1) value (with or without an additional Uncertainty Factor (UF) to account for the small sample size), and/or (2) acute hazard values or additional studies that examine durations of exposure of less than 24 hours to less than 14 days, and/or (3) the odor threshold for 1,3-butadiene.

EPA Response: The EPA has considered the feedback provided and responses to specific recommendations are included in this section. In response to the recommendation, EPA has moved the table of considered acute PODs including irritation (the basis of the AEGL-1), abnormal sternebrae, and dominant lethality from Appendix E-2 of the *Draft Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2024e) to Section 4.2.2.3.1 (Table 4-1) of the final *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d). This section expands the previous justification for not calculating acute risks "because any options would have low confidence and are less protective than the intermediate POD or existing regulatory limits."

1.5.1.1 Comment

Summary: As a bulleted recommendation on page 82 of the SACC report, the SACC recommended that EPA should state whether or not any acute studies were identified through systematic review.

EPA Response: Acute studies were identified in the systematic review process and results are summarized in *Data Extraction Information for Human Health Hazard Animal Toxicology and Epidemiology for 1,3-Butadiene* (U.S. EPA, 2025a). These results are only for mortality based on LD50 (lethal dose for 50% of animals) results and are summarized in Section 4.2.2.3.1 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d).

1.5.1.2 Comment

Summary: As a bulleted recommendation on page 82 of the SACC report, the SACC recommended that EPA review the data underlying the OSHA STEL, in case there is some information on acute exposure, and clarify the basis of the Occupational Safety and Health Administration's Short-Term Exposure Limit (OSHA STEL).

EPA Response: In response to the recommendation, EPA explains in the new Section 4.2.2.3.1 of the Human Health Hazard Assessment that the STEL was derived as five times the OSHA PEL (Permissible Exposure Limit). The PEL is based on cancer, which requires long-term repeated exposure, and therefore the STEL does not indicate support for an acute endpoint.

1.5.1.3 Comment

Summary: Throughout pages 78 to 81 of the SACC report, the SACC noted that EPA should reconsider the determination from the draft that fetal body weight would not result from a single exposure (EPA concluded that the POD for reduced fetal weight observed in a repeated dose study should not be applied to an acute exposure scenario). EPA's risk evaluation for trichloroethylene was quoted as considering developmental toxicity endpoints for acute scenarios, including several references supporting the basis that "repeated exposure is not a necessary prerequisite for the manifestation of developmental toxicity." Additional examples were provided of fetal body weight cited as supporting an acute POD in two pesticide assessments (Quinchlorac and Chlorothalonil; referenced in comment 0425-0120) as well as a study showing effects on fetal weights following exposure *in utero* to a one–time dose (Thaete et al., 2013).

EPA Response: EPA has expanded the justification for not applying the fetal weight results to acute (single dose) exposures in Section 4.2.1.1 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d). While there are several instances of EPA assessments in pesticides and other programs citing fetal body weight as an adverse effect associated with an acute POD, these are almost always associated with binary effects such as mortality (*e.g.*, resorptions, pup death) or teratogenicity (*i.e.*, malformations). For trichloroethylene, acute developmental toxicity endpoints were from prenatal mortality, malformations, and developmental toxicity; decreased fetal weight was not discussed. Similarly, one of the pesticide examples cited, Chlorothalonil, only discusses increased resorptions and post-implantation loss associated with acute exposure and states, "there were no other effects attributable to a single dose observed in the database." Reduced fertility or offspring mortality were not observed following 1,3-butadiene exposure in any study while potential defects were only seen at much higher doses (discussed as potential POD option in Sections 4.2.1.1 and 4.2.2.3.1 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d). The intermediate/chronic POD for fetal weight based on effects seen at the lowest dose therefore is not applicable to a single exposure.

Reduced fetal weight has resulted from a single maternal exposure to certain pain management pharmaceuticals (Thaete et al., 2013), however these results cannot be reliably used for conclusions. These drugs were all administered at elevated therapeutic doses intended to elicit a biological effect. Most were injected; only one of these chemicals was administered externally (isoflurane), for which exposure was at a very high concentration of 3% (30,000 ppm), and bone growth (for the humerus specifically) was more consistently impacted than fetal weight.

The Risk Evaluation for Trichloroethylene did not consider fetal weight relevant to acute exposures. Developmental toxicity endpoints used for acute PODs in that document were prenatal mortality, developmental neurotoxicity, and congenital heart malformations. The citations discussed in that risk evaluation (Davis et al, 2009; Van Raaij et al, 2003, U.S. EPA, 1991, U.S. EPA, 1996) state that "certain developmental effects may result from a single exposure during a critical window of development" (emphasis added). Consistent with the discussion above, reduced fetal body weight was not considered one of those effects.

1.5.1.4 Comment

Summary: The SACC noted on page 81 of the SACC report that no effects were observed over two years following a single 2-hour exposure of mice for up to 10,000 ppm, and a back-calculated 24-hour POD estimate of 416 ppm based on a 1×10^{-6} upper bound estimate of risk may be health protective.

EPA Response: This study (Bucher et al., 1993) only qualitatively reported mortality and body weight along with quantification of cancer incidence over 2 years following the single exposure. Therefore, it would not be appropriate to extrapolate results from this study for identifying sensitive acute effects.

1.5.1.5 Comment

Summary: As a bulleted recommendation on page 82 of the SACC report, the SACC recommended that EPA expand the duration in the definition of acute inhalation toxicity tests to include 24 hours (or shorter), as a 24-hour exposure duration is included in the EPA acute inhalation test guidelines (EPA 1998; EPA 712–C–98–193) (U.S. EPA, 1998). The SACC additionally noted that ATSDR considers acute exposures as durations up to 14 days.

EPA Response: EPA has added bullets explaining each of the duration categories to Section 2 of both the final risk evaluation and the human health hazard assessment. EPA retains existing definitions of acute (≤ 24 hr), intermediate (less than chronic repeat exposure), and chronic (> 10% of lifetime) exposure, adapted from the EPA IRIS glossary (https://www.epa.gov/iris/iris-glossary; accessed December 10, 2025).

1.5.2 Charge Question 5b.i.

On page 23 of the SACC report, the SACC noted that the EPA has carefully described the toxicokinetics of 1,3-butadiene with primary exposure through inhalation, including newly recognized chlorinated and ketone/aldehyde metabolites of which interspecies metabolism differences and adverse effects are unknown. They stated that the description and explanation of these studies was comprehensive, and the information presented reflected the current science.

1.5.2.1 Comment

Summary: In a bulleted recommendation on page 87 of the SACC report, the SACC recommended that EPA consider data that inform understanding of toxicodynamics, and in the narrative indicated that the Absorption, Distribution, Metabolism, and Excretion (ADME) data did not consider the differences in metabolism observed between species. SACC also raised the question of whether variability of

toxicokinetic responses in the human population including sex, ethnicity, age, smoking status, and genetic polymorphisms was considered sufficiently, as these factors may contribute to variation across the human population.

EPA Response: In response to the recommendation, EPA has revised Section 3.3 of the Human Health Hazard Assessment to expand the discussion of toxicokinetics and toxicodynamics, including considerations of human variability. Quantitative comparison of metabolic activation and detoxification are presented for mice, rats and humans. A discussion of the increased toxicodynamic sensitivity of mice compared to rats for ovarian toxicity is also included in Section 4.1.1 of the Human Health Hazard Assessment and the revised section includes human toxicokinetic variability due to sex, ethnicity, glutathione s-transferase theta 1 (GSTT1), genotype, age, and smoking status. A discussion of the increased toxicodynamic sensitivity of mice compared to rats for ovarian toxicity is also included in Section 4.1.1 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d) and the revised section includes human toxicokinetic variability due to sex, ethnicity, glutathione s-transferase theta 1 (GSTT1), genotype, age, and smoking status. Additionally, EPA describes evidence of biological susceptibility and how it was considered in the risk evaluation in Section 7.2 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d). EPA explains how the risk evaluation incorporated PESS considerations into risk estimates in Section 5.3.5 of the risk evaluation, which includes a breakdown of exposures and cancer risks across demographics.

1.5.2.2 Comment

Summary: In a bulleted recommendation on page 87 of the SACC report, the SACC noted that EPA should include information describing relative levels of hemoglobin adducts measured in humans as compared to the other test species and more thoroughly discuss those levels to improve the general reader's understanding of the relative bioactivation of 1,3-butadiene in humans as compared to mice, rats and non-human primates. EPA should also determine if similar DNA adduct information is available and include any available data of this type.

EPA Response: In response to the recommendation, the metabolism section (Section 3.3 in *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d)) has been updated with detailed cross-species comparison of hemoglobin adducts, showing that human DEB (1,2,3,4-diepoxybutane) derived adducts are substantially lower than those in mice or rats at comparable exposures. The section also includes available data on DNA adduct in both human and animals, noting their much lower abundance in humans and the current limitations on their use in quantitative cross-species extrapolation.

1.5.2.3 Comment

Summary: In a bulleted recommendation on page 87 of the SACC report, the SACC recommended that EPA consider all available Physiologically Based Pharmacokinetic (PBPK) models and determine if it would be feasible to develop a reasonable model, informed by the several existing ones. Several references were provided in the SACC report:

1. Bois FY, Brochot C. 2016. Modeling Pharmacokinetics. Methods Mol Biol. 2016;1425:37-62. doi: 10.1007/978-1-4939-3609-0_3. PMID: 27311461.

2. Bois FY, Tebby C, Brochot C. (2022). PBPK Modeling to Simulate the Fate of Compounds in Living Organisms. Methods Mol Biol. 2022;2425:29-56. doi: 10.1007/978-1-0716-1960-5_2. PMID: 35188627.
3. Brochot C, Smith TJ, Bois FY, (2007). Development of a physiologically based toxicokinetic model for butadiene and four major metabolites in humans: global sensitivity analysis for experimental design issues. Chem. Biol. Interact.167 (3), 168–183.
4. Campbell J, Van Landingham C, Crowell S, Gentry R, Kaden D, Fiebelkorn S, Loccisano A, Clewell H. (2015). A preliminary regional PBPK model of lung metabolism for improving species dependent descriptions of 1,3-butadiene and its metabolites. Chemico-Biological Interactions 238: 102–110.
5. Csanady GA, Guengerich FP, Bond JA. (1992). Comparison of the biotransformation of 1,3-butadiene and its metabolite, butadiene monoepoxide, by hepatic and pulmonary tissues from humans, rats and mice. Carcinogenesis 13 (7), 1143–1153.
6. Dahl AR, Henderson RF. (2000). Comparative metabolism of low concentrations of butadiene and its monoepoxide in human and monkey hepatic microsomes. Inhal Toxicol. 200 May;12(5):439-51. doi: 10.1080/089583700196130. PMID: 10880138.
7. Filser JG, Johanson G, Kessler W, Kreuzer PE, Stei P, Baur C, Csanády GA. (1993). A pharmacokinetic model to describe toxicokinetic interactions between 1,3-butadiene and styrene in rats: predictions for human exposure. IARC Sci Publ. 127:65-78. PMID: 8070888.
8. Johanson G, Filser JG. (1993). A physiologically based pharmacokinetic model for butadiene and its metabolite butadiene monoxide in rat and mouse and its significance for risk extrapolation. Arch Toxicol. 67(3):151-63. doi: 10.1007/BF01973302. PMID: 8494494.
9. Johanson G, Filser JG, (1996). PBPK model for butadiene metabolism to epoxides: quantitative species differences in metabolism. Toxicology 113 (1–3), 40–47. DOI: 10.1016/0300-483x(96)03425-7 PMID: 8901881.
10. Kirman CR, Grant RL. (2012). Quantitative human health risk assessment for 1,3-butadiene based upon ovarian effects in rodents. Regul Toxicol Pharmacol. Mar;62(2):371-84. doi: 10.1016/j.yrtph.2011.11.001. Epub 2011 Nov 10. PMID: 22100993.
11. Kohn MC, Melnick RL, (2001). Physiological modeling of butadiene disposition in mice and rats. Chem. Biol. Interact. 135–136, 285–301. DOI: 10.1016/s0009-2797(01)00176-4 PMID: 1139739.
12. Leavens TL, Bond JA. (1996). Pharmacokinetic model describing the disposition of butadiene and styrene in mice. Toxicology. Oct 28;113(1-3):310-3. doi: 10.1016/0300-483x(96)03463-4. PMID: 8901915,
13. Sielken RL Jr, Reitz RH, Hays SM. (1996). Using PBPK modeling and comprehensive realism methodology for the quantitative cancer risk assessment of butadiene. Toxicology. Oct 28;113(1-3):231-7. doi: 10.1016/0300-483x(96)03450-6. PMID: 8901903.
14. Smith TJ, Bois FY, Lin YS, Brochot C, Micallef S, Kim D, Kelsey KT. (2008). Quantifying heterogeneity in exposure-risk relationships using exhaled breath biomarkers for 1,3-butadiene exposures. 2008. J Breath Res. Sep;2(3):037018. doi: 10.1088/1752-7155/2/3/037018. Epub 2008 Sep 8. PMID: 21386179; PMCID: PMC439465511.
15. Smith TJ, Lin YS, Mezzetti M, Bois FY, Kelsey K, Ibrahim J. Genetic and dietary factors affecting human metabolism of 1,3-butadiene. (2001). Chem Biol Interact. Jun 1;135-136:407-28. doi: 10.1016/s0009-2797(01)00180-6. PMID: 11397404.

16. Sweeney LM, Himmelstein MW, Gargas ML.(2001). Development of a preliminary physiologically based toxicokinetic (PBTK) model for 1,3-butadiene risk assessment. Chem. Biol. Interact. 135–136, 303322.

EPA Response: The PBPK section (Section 3.5 in *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d)) has been revised to acknowledge existing models and to highlight their major limitations for quantitative risk assessment. The section now highlights major uncertainties, such as incomplete understanding of alternative oxidation and detoxification pathways, limited validation of *in vitro* to *in vivo* extrapolations, insufficient data on first pass and regional lung metabolism, and unclear kinetics of newly identified bifunctional metabolites. Based on these significant and unresolved uncertainties, EPA has determined that existing PBPK models are currently unsuitable for quantitative human risk assessment of 1,3-butadiene.

1.5.2.4 Comment

Summary: On pages 94-104 of the SACC report, the SACC discussed the complexity of the species differences in metabolites and how that would influence considerations around interspecies UFs/adjustment factors. Mice bioactivate 1,3-butadiene more than rats which bioactivate more than humans. The SACC recommends that the EPA investigate using the relative levels of the total reactive metabolites formed in mice, rats and humans to make interspecies adjustments and consider where a specific metabolite is measured to be many-fold different across species and generate Human Equivalent Concentrations (HECs) using the available data since adverse effects with butadiene are likely the result of these (or subsequently formed) reactive metabolites. They also suggest that EPA could alternatively use data from another non-mouse model; with consideration that the greater sensitivity to the adverse effects of 1,3-butadiene observed in mice reflects plausible modes of action related to the higher production of active metabolites. However, the SACC also acknowledged that is not clear if mice are always 'uniquely sensitive' to 1,3-butadiene toxicity compared to other vertebrates.

EPA Response: The revised metabolism section (Section 3.3) of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d) incorporates available data on reactive metabolite formation across mice, rats, and humans. While mice generally produce higher levels of reactive metabolites and show greater sensitivity for some endpoints, the analysis used a weight of evidence approach considering multiple species to reflect metabolic and toxicodynamic differences. The revised Section 4.2.2.1 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d) further clarifies that a well-defined Mode of Action (MOA) is required for the application of a data-derived uncertainty factor, and an MOA is not supported for non-ovarian toxicity non-cancer endpoints. Robust mechanistic data are lacking for endpoints other than ovarian atrophy. Additionally, high inter-individual and intra-population variability, weak or inconsistent exposure response relationships, detectable background levels in unexposed human populations, limited cohort diversity, and sex-dependent differences reduce confidence in species specific toxicokinetic adjustments. According to EPA guidance for application of data derived extrapolation factors (DDEFs) (U.S. EPA, 2014), a DDEF requires: 1) sufficient information on an endpoint-specific mode of action, 2) data specific to the affected tissue, and 3) identification of the most appropriate dose metric. EPA also agrees that there is limited evidence suggesting that mice are uniquely sensitive for endpoints besides ovarian toxicity.

Because there is insufficient data across all these factors, the agency has determined that derivation of a DDEF to adjust human equivalent concentrations (HECs) is not supported. Therefore, EPA relies on default dosimetric adjustments and uncertainty factors per EPA guidance.

1.5.3 Charge Question 5b.ii.

On page 24 of the SACC report, the SACC agreed that, collectively and given the uncertainties, the proposed MOA was determined to be plausible. There is evidence of significant damage to ovarian function in mice and uncertainties exist when translating these effects to impacts in women. Specific comments regarding ovarian atrophy are addressed below.

1.5.3.1 Comment

Summary: The SACC discussed about the uncertainties in translating mouse findings for ovarian toxicity to humans and, as a bulleted recommendation on page 94 of the SACC report, recommended that physiological variation due to species sensitivity be discussed in the analysis of adverse effects. The interaction of dose and senescence of organ function confounds the interpretation of the outcomes of exposure, while extending the 1,3-butadiene exposure into a late life stage when follicle loss accelerates may diminish the sensitivity for determining diminished ovarian function. Differences in mouse strains could also add to variability, relevant to the variability in the number of primordial follicles at birth in different women. The SACC noted that uncertainties may lead to a conclusion that ovarian atrophy may have disadvantages as an appropriate endpoint for quantitative risk assessment. It was recommended that EPA should also acknowledge physiological variation in the discussion of species sensitivity; The SACC acknowledged that is not clear if mice are always 'uniquely sensitive' to 1,3-butadiene toxicity compared to other vertebrates.

EPA Response: The endpoint of ovarian atrophy was more sensitive than other adverse outcomes and the POD is likely not representative of non-mouse species, which are expected to be less sensitive. EPA acknowledges that human relevance may depend on the toxicokinetic sensitivity of susceptible individuals and has added a statement acknowledging this uncertainty to Section 4.1.1.3.7 of the of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d).

1.5.3.2 Comment

Summary: On page 95 of the SACC report, the SACC noted that ovarian atrophy should not be considered an adverse outcome but instead the last key event leading to the adverse outcome of reduced fertility. It can reasonably be assumed that ovarian atrophy as a result of follicular degeneration would reduce fertility and early reproductive senescence. However, it was noted that evidence of reduced fertility from 1,3-butadiene exposure is not presented in the human health hazard assessment.

EPA Response: While an assumption of reduced fertility as a potential consequence of ovarian atrophy is a reasonable hypothesis, the lack of direct evidence for this outcome does not provide enough evidence to draw that conclusion. For this reason, EPA maintains ovarian atrophy as the adverse outcome. EPA has added discussion about the adversity and biological significance of ovarian toxicity, especially in the absence of evidence for reduced fertility, to Section 4.1.1 of the of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d).

1.5.3.3 Comment

Summary: On pages 89 to 94 of the SACC report, the SACC encouraged EPA to adapt the ovarian atrophy MOA into the Adverse Outcome Pathway (AOP) framework as introduced by Ankley and Edwards (2018). It was suggested that the 1,3-butadiene MOA analysis would benefit from: (1) the exclusion of KE1 (Key Event 1) and KE2 which relate to the toxicokinetic (TK) analysis, (2) the addition of a molecular initiating event (MIE), (3) the modification/replacement and renumbering of KE3 to become KE1, (4) and the addition of two additional steps- one more KE and a postulated adverse outcome that results from ovarian atrophy.

EPA Response: Given the available evidence, there is not enough information to support the SACC-proposed AOP, especially the ultimate adverse outcome. As the SACC noted, their suggested adverse outcome (*i.e.*, fertility, reproductive senescence) is uncertain and "one might conclude that the AO remains unidentified." The basis for the uncertainty is that there is no animal or human evidence of reduced fertility as a result of 1,3-butadiene exposure. Most importantly, AOPs are intended to be chemical agnostic, while the ovarian toxicity MOA describes a chemical- and metabolite-specific MOA for assessing the human relevance of mouse outcomes. It cannot be generalized to other chemicals and serves a purpose specific to this risk evaluation. Because EPA is not applying the Adverse Outcome Pathway (AOP), KE1 does need not to be an MIE. EPA concludes that metabolism to 1,2,3,4-diepoxybutane (DEB) in KE1 is the most important key event in the described mode of action for ovarian atrophy and therefore should not be removed.

1.5.4 Charge Question 5b.iii.

On page 24 of the SACC report, the SACC report agrees that ovarian atrophy is relevant to humans, but that human relevance cannot be reasonably excluded due to conserved metabolic pathways, despite differences in apparent sensitivity.

1.5.4.1 Comment

Summary: The SACC agreed that there is high uncertainty in extrapolating the mouse results to humans, however less sensitivity does not mean a lack of potential damage, and there was a suggestion that extrapolation could be accomplished using an Uncertainty (or "adjustment") Factor less than 1. SACC agrees with EPA on answers to the four questions from the Boobis et al., 2008 Human Relevance Framework except Q1, because SACC expressed some disagreement with ovarian atrophy as adverse outcome. Overall, there was support among the SACC for the EPA's current conclusion that the mouse data are indicative of potential damage but are not directly transferable to human risk assessment due to uncertainties. A specific recommendation was for EPA to retain ovarian atrophy as a relevant non-cancer potential adverse outcome but not to use it in dose response analysis.

EPA Response: Unlike an AOP, an MOA can incorporate an uncertain adverse outcome downstream of the final key event. EPA has added discussion about the adversity and biological significance of ovarian toxicity, especially in the absence of evidence for reduced fertility, to Section 4.1.1 of the of the Human Health Hazard Assessment in response to SACC's bulleted recommendation. EPA agrees that ovarian atrophy is qualitatively relevant to humans and concludes that the mouse POD cannot be extrapolated to humans.

1.5.5 Charge Question 5c.i.

On page 98 of the SACC report, the SACC noted that the process the EPA utilized to identify the most sensitive endpoints and those for which quantitative data were available, were consistent with EPA guidelines. The most sensitive endpoints identified were related to developmental toxicity and the BMD modeling did not indicate HECs that varied much across the endpoints considered. However, more information was requested regarding methods for BMD modeling of the endpoint of choice, fetal body weight**,** as discussed below.

1.5.5.1 Comment

Summary: The SACC report expressed concern that the panel may not have been able to fully evaluate the selection of decreased fetal body weight as the critical endpoint for the developmental toxicity assessment because study selection was limited to relevant studies with effects at the organ level or higher and did not consider biochemical markers or other outcomes at the cellular level. The SACC

highlighted the potential that risks may be increased if more sensitive endpoints were identified. As a bulleted recommendation on page 99 of the SACC report, the SACC recommended that EPA clarify whether the systematic review protocol screened for papers that measured biochemical changes or cellular-level effects and whether these were included in the animal and human evidence streams (or provide a justification for why these cellular-level effects should not be considered). SACC was supportive of the process that the EPA utilized to identify the most sensitive endpoints and those for which quantitative data were available, noting these were consistent with EPA guidelines. To be comprehensive, the SACC recommended that EPA update their systematic review to include studies published after 2019, consistent with TSCA's "best available science" requirement.

EPA Response: EPA notes that it considered biochemical changes, cellular, and sub-cellular effects in the Draft Human Health Hazard Assessment (U.S. EPA, 2024e). For example, the critical hazard outcome of male reproductive and developmental toxicity discusses adverse effects on sperm, and the primary hematological measurements that were discussed indicative of anemia were erythrocyte counts, hemoglobin concentrations, and cell volume. Upon considering all reasonably available information, and consistent with EPA guidelines, EPA determined that decreased fetal body weight is the most sensitive and robust critical endpoint relevant to humans. EPA conclusions are consistent with the best available science.

In 2024, prior to completion of the *Draft Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2024e), EPA updated the literature pool with studies published after the September 2019 literature cutoff date through manual PubMed keyword searching, reviewing key studies and dose-response analyses provided by stakeholders, and backwards searching of references cited in those stakeholder comments. More specifically, EPA searched for recent information on 1,3-butadiene hemoglobin adducts and metabolites to inform the modes of action for each health outcome, and EPA also incorporated all updates to the original occupational cancer cohort (Delzell et al., 1996) to support an updated cancer hazard value; the cancer IUR is based on two 2021 studies (Sathiakumar 2021a,b). The final human health hazard assessment additionally considers all studies (regardless of publication date) that were recommended by the SACC or public commenters. The SACC did not indicate particular studies that provide evidence of missed non-cancer endpoints or potentially increased risks from additional data sources; four studies related to breast cancer were mentioned and have been incorporated into the final risk evaluation. Therefore, EPA concludes that the database supporting the hazard assessment has in fact already been updated with post-2019 studies. When also considering incorporation of the few additional studies recommended by SACC and public commenters, the database is considered fully up to date for the final *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d).

1.5.5.2 Comment

Summary: On page 99 of the SACC report, the SACC recommended that EPA update the main text with a thorough explanation of the detailed information in Appendix B of the Human Health Hazard Assessment (Benchmark Dose Modeling Results) to avoid the need to go through large tables of modeling output, and also to provide additional information in support of methods used in the modeling of the endpoint of choice, fetal body weight.

EPA Response: In response to the request, the recommended model for each BMDL from the table in Appendix B has been added to the main text in the benchmark concentration analysis, Section 4.2.2.2 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d). EPA has now clarified in that section that the hybrid modeling approach was selected because the continuous variable modeling required dropping the top dose and did not allow for a nested analysis. Appendix B contains summary

modeling results for all runs, including rationale for model selection. Additional details are provided in the *Benchmark Dose Modeling Results for 1,3-Butadiene* supplemental document (U.S. EPA, 2025l).

1.5.5.3 Comment

Summary: On page 98 of the SACC report, the SACC noted that the following strengths and limitations of fetal weight as the key endpoint should be considered: Specifically, body weight can be confounded by gestational age, in particular shorter gestational age. Fetal body weight can also be subject to live birth bias, which may be a consideration if 1,3-butadiene increases the risk of miscarriage. Strengths of fetal body weight as an endpoint include ease of measurement, minimal measurement error, and robust literature linking lower birthweight to adverse health outcomes across the lifespan. For these reasons, the SACC noted that is reasonable to assume that fetal bodyweight could be acting as a mediator.

EPA Response: EPA consistently observed effects on fetal weight across multiple studies and species in the absence of fetal mortality. EPA agrees with the strengths of the endpoint, and the strength is enhanced by the fact that all developmental endpoints had similar PODs indicating a consistent threshold for reproductive and developmental effects.

1.5.6 Charge Question 5c.ii

1.5.6.1 Comment

Summary: On page 100 of the SACC report, the SACC recommended that EPA apply the probabilistic dose-response assessment methods of the IPCS to estimate the risk of adverse effects at various levels of exposure (citing WHO IPCS 2009 and 2017, Chiu et al., 2015, Chiu et al., 2018, Blessinger et al., 2020, Chiu et al., 2021). The SACC asserted that MOE approach may have disadvantages for characterizing risk as compared to a probabilistic approach and that the MOE approach may be inconsistent with amended TSCA's requirements to use the "best available science" and to ensure protection of PESS (15 USC 2602(12)). Using a probabilistic approach for deriving a reference value allows quantitative characterization of the severity, incidence, and uncertainty of effects at various exposure levels. Other recommendations as part of a probabilistic approach included conducting sensitivity analyses using different cut points of exposure, such as quartiles or other quantiles. Considering alternative approaches to estimating risk, the SACC suggested that EPA clarify that there is no unreasonable risk at a 1-in-600 probability of adverse effect (estimated based on the POD for fetal body weight and associated uncertainty factors).

EPA Response: EPA has not performed probabilistic dose-response analysis. EPA is in the early stages of research associated with developing probabilistic methods and guidance for use in human health hazard assessment. Until this research is matured and completed, EPA will continue to use the approaches described in existing EPA guidance documents for using default values (U.S. EPA, 2002) and for developing refined values (*e.g.*, 2014 Guidance for Applying Quantitative Data to Develop Data-Derived Extrapolation Factors for Interspecies and Intraspecies Extrapolation; (U.S. EPA, 2014). There is no current policy for determining appropriate regulatory thresholds for results of a probabilistic analysis. Until probabilistic methods are standardized into guidance, the EPA does not wish to speculate on estimates of percent population affected.

1.5.6.2 Comment

Summary: On page 100 of the SACC report, the SACC recommended that EPA consider using a nested model using continuous data, noting their impression that the recently released update of the EPA's BMD software contains a module to facilitate such analysis.

EPA Response: A nested continuous model is in development but is not yet available in the existing BMDS model toolset (https://bmdsonline.epa.gov/; accessed December 10, 2025); the only options available at this time are continuous (non-nested), dichotomous, and dichotomous nested.

1.5.7 Charge Question 5c.iii

On page 25 of the SACC report, the SACC noted that EPA followed the process for selecting BMRs in a manner consistent with the Benchmark Dose Technical Guidance (U.S. EPA, 2012) for the different endpoints (dichotomous versus continuous) considered. However, suggestions for other considerations around modeling the fetal body weight dataset by varying the BMR are discussed below.

1.5.7.1 Comment

Summary: On page 101 of the SACC report, the SACC noted that the EPA followed the process for selecting Benchmark Responses (BMRs) in a manner consistent with the Benchmark Dose Technical Guidance (U.S. EPA, 2012) for the different endpoints considered. SACC requested additional information to support the need for the changes in methodology in the modeling of the endpoint of choice, fetal body weight (*e.g.*, dichotomizing the data). They also suggested expanding discussion in the main text providing rationale and consideration of all modeling decisions without requiring access to all the supplemental BMD modeling results.

EPA Response: Sections 4.2.2.2 and 4.2.2.3 of the Draft Human Health Hazard Assessment (U.S. EPA, 2024e) included details of considerations for modeling decisions including a summary of the results. To address SACC's concern, EPA has added some additional context and explanation to those sections for the final version.

1.5.7.2 Comment

Summary: The SACC noted that the fetal body weight dataset relied upon represents an unusual dataset, with continuous data that has been dichotomized, with a POD outside the observable range of the data, which may warrant the default 10 percent BMR rather than a 5 percent BMR. In addition, the use of a 5 percent BMR for fetal body weight was noted as potentially inconsistent with the BMR applied for maternal body weight changes, which is 1 standard deviation. On page 101 of the SACC report, the SACC recommended that EPA consider using 10 percent BMR rather than 5 percent BMR.

EPA Response: Dichotomizing the fetal weight data is independent of the selection of BMR. EPA evaluated the strengths and weaknesses of the dichotomization approach and determined that dichotomizing reduces uncertainty by accounting for intra- and inter-litter covariates. EPA BMD modeling guidance (2012) discusses this "hybrid approach" and specifically cites the 2002 IRIS assessment of 1,3-butadiene as an example of the approach. Therefore, EPA's approach is wholly consistent with EPA guidance and the history of 1,3-butadiene assessment at the Agency.

A 5 percent BMR for reduced fetal weight is consistent with recommendations from BMD modeling guidance and past EPA approaches for developmental outcomes. EPA explains in Section 4.2.2.2.1 of the *Human Health Hazard Assessment* that the BMD/BMDL (Benchmark Dose lower confidence limit) is within relatively close range of the lowest dose which may not even represent a no-effect level (see comment 1.5.8.1 and response). Additionally, the modeling result using a 10% BMR on the dichotomized dataset based on a 10% cutoff of the probability distribution results in the same value of 2.5 ppm. EPA has updated tables throughout the dose-response section of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d) to refer to the value as BMR_{5or10}.

1.5.8 Charge Question 5c.iv

On page 102 of the SACC report, the SACC supported the use of BMD modeling and supports continuing to use BMD modeling to calculate a BMDL. However, the SACC recommended that EPA consider using probabilistic dose-response assessment methods as summarized below**.**

1.5.8.1 Comment

Summary: On page 102 of the SACC report, the SACC recommended that EPA should continue using BMD modeling to determine the BMDL. This approach considers all study data, can estimate a POD outside of the doses tested including below the lowest dose tested, and minimizes adjustment or uncertainty factors. However, SACC additionally recommended that the EPA should work towards use of probabilistic dose-response assessment methods.

EPA Response: EPA agrees that BMD modeling of the key endpoints has many advantages and will continue to use BMD modeling whenever possible. See response to similar comment 1.5.6.1 about probabilistic dose-response assessment.

1.5.8.2 Comment

Summary: On page 101 of the SACC report, the SACC noted that EPA clarify whether the results from the (Green, 2003) study as a potential POD were considered; however, the SACC also noted that this study was not peer-reviewed and was funded by the American Chemistry Council (ACC). The EPA was also requested to clarify whether the (Green, 2003) analysis influenced the estimation of the BMDL of 2.5 ppm that is relied upon for the margin of exposure comparison in the 1,3-Butadiene Draft Risk Evaluation (U.S. EPA, 2024g).

EPA Response: EPA references the Green (2003) analysis in Section 4.2.2.2.1 to explain the uncertainty in the characterization of the fetal weight response at the lowest dose, where it was determined to be a Lowest Adverse Effect Level (LOAEL) in the original study but was recharacterized as a No Adverse Effect Level (NOAEL) based on the statistical analysis of Green (2003). This uncertainty further supports the benefits of benchmark dose modeling, which considers the entirety of the data in a manner that is agnostic to the statistical significance of a response at any particular dose. The Green analysis therefore had no influence on the BMD modeling results.

1.5.9 Charge Question 5d.i

On page 102 of the SACC report, the SACC agreed that there is strong, sufficient, and robust evidence to conclude that 1,3-butadiene causes cancer through a mutagenic mode of action. The Committee agrees with the EPA's conclusion that a Mutagenic Mode of Action (MMOA) underlies the carcinogenic response observed in various target organs/tissues in both laboratory animals and humans. In addition, it was noted by the SACC that the identification and support for key events in the carcinogenesis of 1,3-butadiene clearly presents the mutagenic MOA evidence. The SACC commended EPA for clearly stating, providing transparency: "1,3-butadiene is carcinogenic through metabolism into direct-acting mutagens."

1.5.9.1 Comment

Summary: On page 111-112 of the SACC report, the SACC recommended EPA to remove reference to Chronic Myeloid Leukemia (CML) and refer instead to cancer more broadly as this effect has weakened with time, referencing a lag time of 10 years inconsistent with the lifetable analysis. The panel further recommends including any data on carcinogenicity for specific metabolites and adding information on analogous chemicals with MMOA through epoxide metabolites to strengthen coherence. The SACC report also listed a few typographical errors and suggested minor editorial updates.

EPA Response: The MMOA section (Section 5.3 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d)) has been revised based on the suggested editorial and technical recommendations. The temporality section has been updated to clarify the CML lag time discussion and provide rationale for using 0- year lag time in lifetable analysis. Information on the carcinogenicity of specific metabolites, particularly DEB and EBD, has been incorporated. The coherence section was revised to include information on analogous chemicals with mutagenic modes of action through epoxide metabolites, including structurally related olefins and other epoxide-forming chemicals. All identified typographical and grammatical errors have been corrected as requested.

1.5.9.2 Comment

Summary: On page 104 of the SACC report, the SACC suggested that the EPA investigate using the relative levels of the total reactive metabolites formed in mice, rats and humans to make interspecies adjustments. Further, there was a suggestion to consider where a specific metabolite is measured to be many-fold different across species and generate HECs using the available data given that most adverse effects with butadiene are linked to the result of these (or subsequently formed) reactive metabolites.

EPA Response: See response to similar comment 1.5.2.4.

1.5.9.3 Comment

Summary: On page 103 of the SACC report, the SACC noted that EPA's use of a linear dose-response approach to estimate low dose risks and the use of ADAFs are consistent with the EPA's cancer risk assessment guidelines. However, the SACC suggested that EPA might apply an additional adjustment factor of 10 for pregnant women in fenceline communities, as well as pregnant workers. It was suggested that the prenatal exposure should be also acknowledged and discussed in the final draft risk evaluation in consideration of potential additional sensitivity.

EPA Response:
EPA follows agency guidance in consideration and application of uncertainty factors. Uncertainty factors are not applied to cancer risks, which conservatively use a linear slope down to zero and in the case of 1,3-butadiene also incorporate age-dependent adjustment factors to account for increased susceptibility of children. Both the IUR and lifetime exposure estimates are calculated starting at birth only. Including the third trimester in the adjusted period would also not have any significant mathematical effect since it would be 3 months integrated into more than 78 years of exposure.

EPA does not apply an additional factor for pregnant women, and additional susceptibility factors beyond ADAFs are not applied to linear cancer values per EPA *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005a). Because EPA's Supplemental Guidance for Assessing Susceptibility from Early-life Exposure to Carcinogens (U.S. EPA, 2005b) explicitly excludes in utero exposure from quantitative ADAF adjustments, no additional 10-fold factor is applied for pregnant women or fetuses.

1.5.9.4 Comment

Summary: On page 102 of the SACC report, the SACC agreed that there is strong and sufficient—indeed robust—evidence to conclude that 1,3-butadiene causes cancer through a mutagenic mode of action. The large amount of mutagenic evidence supports a mutagenic mode of action (MMOA) for other tumor types as well. On page 111 of the SACC report, the SACC recommended that EPA change text from "insufficient evidence" to "less evidence" for other cancer types. On page 106 of the SACC report, the SACC noted that EPA should provide additional detail on the potential role of cell proliferation but provides little detail on mechanism and where it may fit in the MOA. A brief summary

of the increased incidences of mutated oncogenes and tumor suppressor genes was requested to be included in discussing mechanisms driving cell proliferation.

EPA Response: EPA has revised the terminology for other tumor types to "less evidence" in accordance with the SACC's recommendation. The mode of action section (Section 5.3 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d)) has been updated with additional detail on cell proliferation and mutations in oncogenes and tumor suppressor genes, as requested.

1.5.9.5 Comment

Summary: On pages 106-111 of the SACC report, the SACC noted that the MMOA would benefit by being reformatted into the more contemporary Adverse Outcome Pathway (AOP) construct that is explicit about the resulting adverse outcome. The AOP would potentially provide more detailed, structured, complete information, with at least two KE for DNA damage and formation of chromosomal aberrations/mutations. The Molecular Initiating Event (MIE) would be the interaction of epoxide metabolites with DNA, and the adverse outcome would be cancer.

EPA Response: The MMOA section (Section 5.3 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d)) has been revised to incorporate the Adverse Outcome Pathway (AOP) framework, as recommended. The updated section acknowledges that the key events align with established AOPs for genotoxic carcinogens that involve DNA-reactive metabolites. It incorporates OECD AOP principles, while maintaining a chemical specific focus on 1,3-butadiene. Specific AOP references have been added, including Event ID 97 for DNA adduct formation and damage, and Event ID 1636 for chromosome aberrations and mutations. The updated section also provides clarification regarding which key event aligns with existing AOP-Wiki entries and includes justification for those key events where standalone AOP Event IDs are not available.

1.5.9.6 Comment

Summary: On page 104 of the SACC report, the SACC noted that the EPA made an overall judgment of "indeterminate/ no effect" for mammary tumors based on human evidence. However, it was pointed out that the standardized mortality results from (Sathiakumar et al., 2019) compared workers to the general population (emphasis added), which does not account for the healthy worker effect; instead, it was suggested that workers should have been compared to an internal control worker population. The study indicated a small number of deaths from breast cancer, which may lead to low power. However, animal data show species concordance with increases in mammary tumors in mice and rats with 1,3-butadiene exposures, raising concerns for breast cancers in humans.

EPA Response: EPA reviewed and analyzed the breast cancer epidemiological studies in Section 5.1.1.4. Based on the results of these cohort and case-control epidemiological studies, only one study showed a statistically significant association between 1,3-butadiene exposure and breast cancer. Given evaluation of the weight of evidence, there is no strong coherence. After considering the animal toxicological, mechanistic, and epidemiological studies, the overall weight of scientific evidence evaluation for the association between 1,3-butadiene exposure and breast cancer is slight.

1.5.10 Charge Question 5e.i

1.5.10.1 Comment

Summary: On page 113 of the SACC report, the SACC disagreed with eliminating the consideration of bladder cancer related to 1,3-butadiene and suggested that this elimination is not supported by the existing science. On page 115 of the SACC report, the SACC recommended that bladder cancer be

included in the cancer risk assessment. The SACC noted that epidemiologic research identified consistent and strong effect of 1,3-butadiene on the incidence of bladder cancer. The weaknesses of not using bladder cancer for risk estimation include the lack of use of the best science available, the lack of integration of the identified cancer burden in this population, and necessarily diminished magnitude of the risk for considering just one of the potential malignancies related to 1,3-butadiene exposure. For both leukemia and bladder cancer, it was suggested that there is a similar quality of data to support the parameter and the inference. On page 126 of the SACC report, as a bulleted recommendation, the SACC recommended that as an alternative to estimating risk from bladder cancer, EPA should consider adding an "uncertainty factor" to compensate for the bias of excluding this outcome.

EPA Response: EPA has combined bladder and leukemia risk for the final risk evaluation. The updated occupational unit risk and overall inhalation unit risk now incorporate the risk of both cancers.

1.5.10.2 Comment

Summary: On page 114 of the SACC report**,** the SACC expressed concern regarding the Cox regression model selected. EPA focused on the regression model that was significant for bladder (Model 4); however, Model 5 was considered the most appropriate model for the leukemia analysis. The SACC noted that additional justification should be provided for focusing on one model versus the other.

EPA Response: Leukemia and bladder cancer have different etiologies, cancer progression, and survival rates, so suitable models selected for leukemia and bladder cancer, respectively, are different. Sections 5.3.9.1 and 5.3.9.5 discuss the reasoning behind selecting the appropriate statistical model, and they are as follows:

(1) Purpose of Inhalation Unit Risk (IUR) derivation: The purpose of IUR derivation is for 1,3-butadiene exposure and bladder cancer; the first three models that include the unexposed population are not under consideration.

(2) Statistical significance in the statistical model: Between models 4 and 5, the model with a statistically significant result is selected.

(3) Two of the reasons to select the beta-coefficients of the fifth model for leukemia are described below:

(a) The previous study results support the use of exposure person time less than or equal to 95 percent in three aspects below:

i. At high exposure levels: (i) Excluding greater than 95 percent exposure person time can reduce the impact of exposure outliers (Sathiakumar et al., 2015; Cheng et al., 2007), and (ii) greater misclassification for jobs entailing higher exposures than for jobs with lower exposures according to the validation investigation at the largest study plant (Sathiakumar et al., 2007).

ii. At low exposure levels: Exposure-response curves tend to dimmish at higher exposure levels. IUR represents a lower exposure range (Stayner et al., 2003), so the concern about high-exposure workers is not as relevant to IUR derivation.

iii. Model fitting performance: Cheng et al. (Cheng et al., 2007) showed stronger exposure-response trends for butadiene and leukemia in analyses while excluding exposures above the 95th percentile.

(b) Better model fitting of Sathiakumar et al. (2021b). Sathiakumar et al. (2021b) showed more robust model fitting than other models and stated, "Trimming to restrict data to ppm-years greater than 0 and less than or equal to the 95th percentile (1,144 ppm-years) of all leukemia decedents yielded a somewhat stronger exposure-response trend for butadiene (trend p=0.016)."

1.5.11 Charge Question 5e.ii

1.5.11.1 Comment

Summary: On page 116 of the SACC report, the SACC noted that the self-censoring of exposure data by incorporating lag time may diminish statistical power somewhat but will reduce bias. The SACC noted it was difficult to identify the parameters included in the modified lifetable analysis (table Beta inputs bladder cancer) in the Sathiakumar et al. (2021a) paper, but 0 years lag is not included, and the authors do not show the criteria for identifying the superior model. Looking at the lifetable, the beta coefficient, and the upper confidence bound is highest when considering a 20-year lag and still statistically significant despite the reduced numbers of samples/year being quantified. In that study, it is observed that working >10 years, and more clearly >20 years provide a consistent relative risk. Given these two considerations, SACC offers disagreement on the use of 0 years for lagging of bladder cancer and instead, as a bulleted recommendation, to use 20 years, consistent with the (Clin et al., 2014) study.

EPA Response: EPA disagrees with this recommendation for the following reasons:
(1) the model from (Sathiakumar et al., 2021a) that EPA determined was most appropriate for adopting the beta coefficient (see comment above) for lifetable analysis used the lag of 0 years and parameters cannot be selectively interchanged across models as the modeling results come from the publication and cannot be re-parameterized by EPA;
(2) the modeling of different lag times in exposure showed little effect on beta coefficients, potentially because the SBR cohort study had been followed for many years post-exposure. Additional detailed reasoning is provided in the text under subsection "A. Data Input" in Section 5.3.9.6 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d).

1.5.12 Charge Question 5e.iii

1.5.12.1 Comment

Summary: On page 117 of the SACC report, the SACC recommended that EPA should apply an additional adjustment factor to account for increased risks of breast cancer if not directly deriving breast cancer risk.

EPA Response: See response in similar comment 1.5.9.6. Applying an additional adjustment factor is not necessary because there is only slight association between breast cancer and 1,3-butadiene exposure.

1.5.12.2 Comment

Summary: On page 117 of the SACC report, the SACC recommended that EPA consider the following breast cancer studies after 2022 (comment 0425-0119) in an updated weight of evidence analysis:

1. Cardona, B., Rodgers, K. M., Trowbridge, J., Buren, H., & Rudel, R. A. (2024). Breast Cancer-Related Chemical Exposures in Firefighters. *Toxics*, *12*(10), 707. https://doi.org/10.3390/toxics12100707
2. Ellis, ET; Young, SG; Carroll, R; Stahr, SD; Runnells, GA; Grasmuck, EA; Su, LJ; Park, Y-MM; Hsu, P-C. (2025). Carcinogenic air pollutants and breast cancer risk in the Arkansas rural community health study: A nested case-control study. 368: 125709. https://www.sciencedirect.com/science/article/pii/S026974912500082X
3. Heck, JE; He, D; Wing, SE; Ritz, B; Carey, CD; Yang, J; Stram, DO; Le Marchand, L; Park, SL; Cheng, I; Wu, AH. (2024). Exposure to outdoor ambient air toxics and risk of breast cancer: The multiethnic cohort. 259: 114362. https://www.sciencedirect.com/science/article/pii/S1438463924000439

4. Kay, JE; Brody, JG; Schwarzman, M; Rudel, RA. (2024). Application of the Key Characteristics Framework to Identify Potential Breast Carcinogens Using Publicly Available in Vivo, in Vitro, and in Silico Data. Environmental Health Perspectives. Volume 132, Issue 1. CID: 017002. https://doi.org/10.1289/EHP13233

EPA Response: EPA has reviewed the relevance of these studies for updating the 1,3-butadiene human health assessment. Cardona *et al.* is a literature review and does not provide new information specific to 1,3-butadiene. Kay *et al.* is a general mechanistic study suggesting applying the key characteristics framework to breast cancer evaluation but does not include specific information about 1,3-butadiene. Ellis *et al.* and Heck *et al.* provide novel epidemiological information, described in Section 5.1.1.4, and these have been incorporated into the final human health assessment as suggested.

1.5.12.3 Comment

Summary: On pages 129-130 of the SACC report, the SACC suggested that the EPA provide more details explaining considerations of selecting one model vs another, *e.g.*, on what other information such as differences in etiology etc., that inform the model choices, clarity of text describing the data adjustments and lifetable analysis, including dosimetric and duration adjustments.

EPA Response: See response for similar comment 1.5.10.2. More details on dosimetric and duration adjustments have been added to Section 5.3.9.2 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d) and 5.3.1.3 of the risk evaluation. Leukemia and bladder cancer have different etiologies, cancer progression, and survival rates, so suitable models selected for leukemia and bladder cancer, respectively, are different. As requested by SACC, more details are described in Sections 5.3.9.1 and 5.3.9.5, which list the reasoning for EPA's selection of the appropriate statistical model as follows:
Purpose of Inhalation Unit Risk (IUR) derivation: The purpose of IUR derivation is for 1,3-butadiene exposure and bladder cancer; the first three models that include the unexposed population are not under consideration.
Statistical significance in the statistical model: Between models 4 and 5, the model with a statistically significant result is selected.
Better model fitting: Two of the reasons to select the beta-coefficients of the fifth model for leukemia are (a) previous study results before Sathiakumar et al. (2021b); and (b) better model fitting of Sathiakumar et al. (2021b).

1.5.13 Charge Question 5f.i

1.5.13.1 Comment

Summary: On pages 119-121 of the SACC report, the SACC noted that the first report of the Alabama cohort (the 1996 papers) included 6 of the 8 Hopkins plants, representing the same cohort. The SACC noted that no explanation was provided to explain why there was a replacement of two different plants. Survival rates have improved over time, so the relationship between 1,3-butadiene and mortality will be less obvious later in a subject's lifetime over the length of this cohort. The longest follow-ups identified a much larger number of deaths but also represent a reduced proportion of all the incident leukemia cases that eventually survived (or died from other causes). Additionally, the Alabama cohort used state mortality data (NIOSH and Hopkins studies used national data) with higher baseline mortality, reducing the possibility of identifying excess mortality when constructing a modified life table analysis. It is not clear in (Sathiakumar et al., 2021b) how they used the individual-level exposure data, but this might have potentially biased the results toward a flatter slope. All these factors appear to be designed to reduce the magnitude of the impact of the relation of 1,3-butadiene with leukemia and is the general

direction of the bias in the estimation. For this reason, SACC recommended that EPA acknowledge a bias and consider applying an "uncertainty factor" to compensate for this bias away in ensuring health protective analyses.

EPA Response: It is not known why there would be a difference in facilities used across different studies, but the U.S.-Canadian styrene-butadiene rubber (SBR) cohort used for EPA's cancer assessment was consistent across the 40+ years of follow-up. EPA used chronologically matched national mortality and incidence data from CDC (CDC, 2024) and NCI (2024), respectively, in the lifetable analysis for calculating the extra risk of leukemia incidence per unit of 1,3-butadiene exposure. The IUR calculation used an exposure-response model for leukemia deaths from (Sathiakumar et al., 2021b) adjusted based on survival rate from these sources. Therefore, EPA's IUR was not affected by any potential biases in the original dataset due to mortality rates. EPA guidance additionally does not support adding uncertainty factors to linear cancer hazard values.

1.5.13.2 Comment

Summary: On pages 119-121 of the SACC report, the SACC noted that there are several sources of uncertainty that exist in the 60-year SBR cohort publications and reports that are worth considering in deciding which cohort and exposure estimates to use:

- The only study that used just monitored data was NIOSH. Others had a combination of job matrix occupational descriptions, exposure estimation, and area and personal monitoring data. Initial reports used monitored data with extrapolation for missing information ((Matanoski et al., 1997) with personal monitoring; (Delzell et al., 1996); (Macaluso et al., 1996) with personal and area monitoring). Subsequent reports used Macaluso data modeled since 2000, and published in 2004 (Macaluso et al., 2004).
- When adjudicating the modeled data to individuals' job histories, the cumulative exposure measured in ppm-years was substantially higher in the updated study (and the sequence of reports). The comparison between the 1996 and 2004 Macaluso reports is substantial. For risk estimation, this could influence, as a "higher butadiene concentration" would be required to reach the same effect. Furthermore, in their initial display of data, they use the mean as the central tendency metric when the distribution of exposures is highly skewed, and the median or might be better. This might be a factor influencing on higher concentrations than what NIOSH identified.
- As the cohort matures, mortality increases and the "healthy worker effect" of the initial analysis is expected to be reduced, and the increased risk persists.
- As the exposure estimate method changed, so did the analysis, with internal comparisons using Cox Proportional Hazards, and mostly using penalized spline regression that "reduces assumptions about the form of the 1,3-butadiene exposure–response curve, in particular, accommodates different exposure–response slopes" (Cheng et al., 2007).
- The SACC noted it is hard to argue against the strength of a substantially larger cohort, despite demographic differences impacting the risk estimates. The inclusion of women and the longer follow-up is desirable. The latest update also added bladder cancer risk and the bias from the comparison is reduced by the use of Cox Proportional Hazards with the internal comparisons.
- Strengths of the 2004 Macaluso study include providing detail in area characteristics, site visits, interviews, and measurements. However, it is not clear how many (if any) of the measurements were personal monitoring data. It seems from the paper that they used area data to estimate workers' exposure. NIOSH, in their 2-plant study (Meinhardt et al., 1978; Meinhardt et al., 1982) collected personal monitoring, and Matanoski et al. (1997) used available personal exposure data. Macaluso explained that while the Hopkins ranking approach in their nested case-control study was pertinent, they wanted to provide quantifiable data usable for risk assessment.

Macaluso identifies very interesting temporal concentrations changes, where most facilities had similar air concentrations until the 1980s when industrial and other changes led to lower concentrations.

- Uncertainty has to be managed in the risk assessment concerning the magnitude of ppm-years, maybe considering an uncertainty factor on the magnitude. Any slope is expected to be about the same.

The SACC additionally provided a table of immediate, medium-, and long-term recommendations. Some of these suggestions include that: EPA should critically review how estimated exposures were assigned based on job matrix, identify any potential problems, and consider redoing the exposure assignment. EPA was encouraged to independently reanalyze the cohort datasets provided by ACC and independently validate any government data as well to develop a summary of different cohort reports of exposures. While the SACC acknowledged the benefits of the updated cohort dataset, at least one member recommended not relying on the Macaluso analysis for worker exposure estimates. Another suggestion was to attempt a sensitivity analysis of different alternatives.

EPA Response: EPA agrees that there are both strengths and weaknesses of the exposure assessment underlying the cancer dose-response modeling. Data inputs and model parameters are not available for review from these studies, and there would not be any measured data from the earlier decades of the cohort (pre-1970) to which they could be compared. Similarly, a sensitivity analysis of limited, outdated datasets that do not represent best available science would not provide additional value to the assessment. However, EPA has thoroughly reviewed the methodology underlying the exposure estimates for the cancer cohort and concluded that Macaluso 2004 is the most appropriate and best available science when considering all the points made above. In short, monitoring data were only available for the 1970s and 1980s, while the cancer cohort covers the 1940s through 2009, so modeling to estimate changes in exposure over time was always required. Macaluso 2004 improves upon the assumptions and data sources used in Macaluso 1996 and uses monitoring data to inform the modeling estimates. EPA identified the research publications of Sathiakumar (2021a,b) as the dose-response analyses representing the best available science for deriving the IUR. This research (Sathiakumar, 2021a,b) used the exposure assessment developed by Macaluso (2004). Therefore, Macaluso (2004) provided the most appropriate exposure data for the dose-response relationship, which in turn was used to derive the IUR. EPA has added a more thorough discussion of the exposure estimation methodology to Section 5.3.7.1.2.

1.5.13.3 Comment

Summary: On page 116 of the SACC report, the SACC acknowledged that studies in the epidemiological cancer cohort were funded by the International Institute of Synthetic Rubber Producers, American Chemistry Council and Styrene Information and Research Center and suggested that these sources may have a potential conflict of interest and a potential source of bias. It was suggested that EPA establish a specific method for addressing industry-sponsored research.

EPA Response: EPA performs a robust systematic review of all data considered for the risk evaluation using consistent data evaluation criteria that include consideration of risk of bias. EPA carefully evaluates all assumptions and interpretations from submitted studies and does not rely on the interpretations of study authors. However, all data are given equal consideration and EPA consistently applies a rigorous process to all data sources.

1.5.13.4 Comment

Summary: On page 130 of the SACC report, the SACC agreed with EPA on the critical effect (leukemia) and the use of an occupational cohort.

EPA Response: EPA agrees that leukemia is the driver for cancer risk. The cancer hazard values now also incorporate bladder cancer in the final risk evaluation.

1.5.13.5 Comment

Summary: On pages 132–133 of the SACC report, the SACC noted that the use of Cox's Proportional Hazards model is pertinent; Sathiakumar et al. (2021) does not provide the actual likelihoods for the different models to assess selection criteria, but the EPA chooses one that includes every hourly worker. SACC noted there may be drawbacks in the approach as all workers may be associated with higher butadiene exposure; even if the likelihood statistic would point to a better model, from the analytical perspective, this might not be desirable.

EPA Response: EPA selected the best available cohort study, which is the SBR cohort with more than 60 years of follow-up data, to investigate the association between 1,3-butadiene exposure and leukemia. In this SBR cohort study, EPA selected the best available publication (Sathiakumar et al., 2021) in this cohort study to conduct the lifetable analysis and derive the IUR. This publication listed several reasons, *e.g.*, previous study results and statistical model fitting (described in its paragraphs "Statistical analysis" of the section METHODS on page 860), to explain the different models. Even though actual likelihoods are not one of reasons, the authors provided sufficient statistical evidence to support the different models.

The design of the SBR cohort study included hourly workers and salaried workers. (Sathiakumar et al., 2021b) described the exposure assessment method in its section METHODS on page 860 as "Exposure estimation entailed identifying for each plant-specific work area/job-specific and time-specific average exposure indices (8-hour time-weighted average concentration in ppm) and compiling these into job-exposure matrices; and linking the time-specific and work area/job-specific exposure estimates in the job-exposure matrices with each employee's work history to obtain cumulative exposure estimates as of each day of follow-up." This method resolves the concerns of this SACC comment, which is to link higher butadiene exposure to all workers. In conclusion, EPA selected the best available science (Sathiakumar et al., 2021b) to derive the 1,3-butadiene IUR.

1.5.13.6 Comment

Summary: On pages 162–166 of the SACC report, the SACC had several general concerns about the selection of the references, including that the systematic epidemiologic literature review omits details on study design, a major criterion for inclusion of any paper. Consequently, the papers were not subjected to a complete critical analysis of how the study design might have introduced bias, allowing conclusions that are not consistent with a well-conducted systematic review. The review did not discuss potential for conflict of interest. A way to statistically deal with the healthy worker effect is to consider internal comparisons within the same cohort population (see Chowdhury et al., 2017). This has the additional advantage of allowing for further data collection and analysis. The Johns Hopkins cohort researchers attempted a nested case-control study design that helped in more accurate validation of the pathology diagnosis, identifying the cases in underlying and contributory causes, and gaining more precision in the work histories. With this design, it was possible to identify the risk ratio for leukemia with greater precision, first with a matched design (Santos-Burgoa et. al, 1992), and later with unmatched and with the use of monitoring data, where available (Matanoski et al., 1997).

EPA Response: In the EPA systematic review for the epidemiological studies (U.S. EPA, 2021), "Analysis" is one of the evaluation criteria in the evaluation form, and it assesses the study design and method, reproducibility of analysis, and statistical models. In addition, Section 5.3.7.3 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d) compares the study design, regression coefficient, and statistical power among the publications of the SBR cohort study and other ecological and case-control studies to select the best study for IUR derivation.

1.5.13.7 Comment

Summary: On page 126 of the SACC report, The SACC recommended that EPA perform a critical review of the validation report from a single Canadian plant (Sathiakumar et al., 2007) and any other validation documents.

EPA Responses: EPA directly compared the monitoring and modeling data for the same period of time and found that the use of modeling data is supported by the validation. The analysis of monitoring and modeling data is addressed in Section 5.3.7.1.2.

1.5.14 Charge Question 5f.ii

1.5.14.1 Comment

Summary: The SACC noted that in general, use of Cubic Spline regression permits an assessment of variabilities across the distribution. This is particularly important to "see" when the mechanism of the toxicity is thought to be acute to the target (consistent with the toxicology for 1,3-butadiene). Use of the 95^{th} percentile is consistent with principles of general practice/policy for the mathematics for the point of risk assessment interest. Hence, considering the Mode of Action for 1,3-butadiene, these statistical approaches are preferable to regression analysis without Cubic Spline modeling. However, this analysis model could be very sensitive to changes in the underlying data, which makes consideration of data for uniquely sensitive life periods or subpopulations important. Consider the challenge of methods (sensitivity and validation) used over decades of data collection when incorporating the data across a wide range of studies and data sets.

As a bulleted recommendation on page 128 of the SACC report, the SACC recommended that EPA should clearly state the rationale for use of the Cubic Spline model or consider alternative approaches based on the available data. There should also be some clarification whether the cubic spline regression was actually used in the models that generated the β -coefficients are presented in Table 5-7, derived from the (Sathiakumar et al., 2021b) paper as the model details are unclear. Relying on the exposed person time rather than including the zero exposed time could be appropriate as it is preferable to incorporating people and person-time where no exposure occurs.

EPA Response: EPA conducted a systematic review for epidemiological studies and identified that the SBR cohort study, including more than 60 years of follow-up data and large male and female study populations (16,579 men and 4,508 women), has the most abundant data to derive 1,3-butadiene IUR. EPA describes the selection of studies and endpoint derivation for dose-response assessment in Section 5.3.7. The data from the SBR cohort study provide the causal association between 1,3-butadiene exposure and cancer. EPA has contacted the authors of the (Sathiakumar et al., 2021b) to confirm whether the cubic spline regression was used in the models that generated the β-coefficients. However, the authors did not respond to EPA. To avoid confusion, the reference to "cubic spline regression" is removed from Table 5-8 and the context in Section 5.3.9.1 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d).

1.5.14.2 Comment

Summary: On page 127 of the SACC report, the SACC noted that the use of the 95th percentile in the distribution of exposure data and the corresponding β coefficient is appropriate for two reasons. First, as was indicated in the original paper (Sathiakumar et al., 2021b), there was greater misclassification in jobs that entailed higher exposures than for jobs with lower exposures and excluding the 95th percentile reduces the impact of those outliers. Second, there is increasing evidence from other exposures and cancer risk that at very high exposure concentrations, the slope of the exposure-response is dampened.

EPA Response: EPA appreciates the SACC committee's agreement regarding EPA's model selection.

1.5.15 Charge Question 5f.iii

Starting on page 128 of the SACC report, the SACC identified some general strengths of the lifetable analysis including the basis in U.S. age-specific population data, as well as consistency with other agencies and strengths of the internal review to find and correct an error. There were some corresponding limitations noted that are addressed in the comments below.

1.5.15.1 Comment

Summary: On pages 128–131 of the SACC report**,** the SACC identified some general strengths of the lifetable analysis including the basis in U.S. age-specific population data, consistency with other EPA offices and agencies, and strengths of the internal review to find and correct an error. Use of lifetable analysis is recommended if the data sets are relatively complete and with appropriate adjustments for age and duration of exposure. SACC also noted the following important limitations in the underlying data and gaps in the discussion, in addition to previous comments: 1) choices of models to determine the beta coefficients to use in the lifetable calculations lacked adequate justification, and 2) variability in the number of individuals and specific information about them, although this is unavoidable. There was also a question of whether the EPA implemented "appropriate adjustments from occupational or general population studies in the lifetable analysis" as was stated in the human health hazard assessment. If so, the SACC requested that these adjustments be explained.

EPA Response: In the lifetable analysis, data of the dose-response relationship between 1,3-butadiene exposure and cancer is needed to calculate the cancer hazard rate. This computation of cancer hazard rate is shown in column K in the lifetable (U.S. EPA, 2025e). EPA identified an appropriate β-coefficient presenting the dose-response relationship between 1,3-butadiene exposure and cancer for leukemia and bladder cancer from the models in (Sathiakumar et al., 2021b) and (Sathiakumar et al., 2021a), respectively. The selection of these β-coefficients is based on the criteria of study and model selections in Sections 5.3.7, 5.3.9.1, and 5.3.9.5 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d).

The variability in the number of individuals and specific information about these statistical models in (Sathiakumar et al., 2021b) and (Sathiakumar et al., 2021a) are due to the various purposes of these models. For example, each publication has 5 statistical models with different conditions, including (1) all person-time (untrimmed, including unexposed, lag time = 0 year), (2) all person-time (untrimmed, including unexposed, lag time = 10 years), (3) all person-time (untrimmed, including unexposed, lag time = 20 years), (4) exposed person-time (exclude unexposed), and (5) exposure person time ≤ 95th percentile. As the SACC mentioned in their comments, this variability is unavoidable.
In response to the SACC's review, additional details on exposure factors implemented into the lifetable analysis are described in Section 5.3.9.2 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d). The selected parameters represent the best available science considering the reasonably available information while maintaining consistency with EPA guidance and other TSCA

risk evaluations. Additionally, a new section providing a comparison between the assumptions and adjustments incorporated into the exposure and hazard values has been added in Section 5.3.1.3 of the risk evaluation.

1.5.15.2 Comment

Summary: On page 131 of the SACC report, the SACC recommended EPA to consider the challenge of methods (sensitivity and validation) used over decades of data collection when incorporating the data across a wide range of studies and data sets. And that utilization of the data from NCI and other curated sources should reduce some of the intra study variability in the occupational exposure results.

EPA Response: Curated data sources, including NCI, may have valuable data which can reduce variability, but it is uncertain whether these data can establish the causal association within a particular cohort, and it is unclear why these data would reduce overall variability.

1.5.15.3 Comment

Summary: On page 127 of the SACC report, the SACC noted that the choice of the 0 lag is also appropriate as it best reflects the known latency period for other leukemogens, although it should be noted that other latencies produced similar coefficients. It is consistent with the empirical data of the underlying study (Sathiakumar et al., 2021b) and with minimum latency determined by NIOSH (2015) for leukemia in the World Trade Center Health Program.

EPA Response: EPA agrees with the SACC conclusion and has used an assumption of 0 years of lag in the lifetable assessment for leukemia risk.

1.5.15.4 Comment

Summary: On pages 130–131 of the SACC report, the SACC noted that with regard to the data set, several decisions could be included as a sensitivity analysis: 1) Use of the full versus censored data set, 2) use of HITS (peak intensity in model), 3) use of the NIOSH measured versus 2004 modeled estimates for the dose-response. 4) Excluding the low end of the data range, and 5) Use of BMR 1 percent versus a much lower level based on power of the study in accordance with EPA BMDS guidance. The SACC suggests it is not necessary to choose the same modeling approach for the different cancers (leukemia, bladder) as there are important differences in the etiology of these cancers (*e.g.*, strength of association with smoking, known longer latency periods for bladder cancer) that may inform different choices. However, modeling choices should be consistent with the EPA guidance and practice.

EPA Response: EPA acknowledges the variability of parameters, however, the values of these parameters that EPA selects represent the best available science. EPA did not conduct the sensitivity analyses for each of the five parameters described by the SACC committee for the following reasons:
1) Full versus censored data set
EPA does not have the data required for a sensitivity analysis suggested by SACC. EPA sent an email to the authors on Sathiakumar et al. (2021b) on May 27, 2025, with a request to confirm the statistical analysis section of this publication, which mentions both regular or multivariable Cox regression and restricted cubic spline Cox regression but has not received a response.

2) Use of HITS (peak intensity in model)
EPA epidemiologists do not agree with the inclusion of 1,3-butadiene high-intensity tasks (*i.e.*, tasks with exposure ≥100 ppm 1,3-butadiene) as a covariate, called "peak exposure," to adjust for the relationship between cumulative 1,3-butadiene exposure and leukemia mortality. Macaluso et al. (2004) reported that peak exposure accounted for a large portion of cumulative 1,3-butadiene exposure in the

SBR worker cohort. Exposure, peak or otherwise, is the main variable in the exposure-response relationship for 1,3-butadiene and leukemia mortality. Treating peak exposure as a covariate removes peak exposure values from cumulative exposure, which is statistically inappropriate. This would reduce the effect of exposure to 1,3-butadiene on leukemia mortality. Please see Section 5.4.1.1.3.

3) Use of the NIOSH measured versus 2004 modeled estimates for the dose-response.
Fajen et al. (1990) published the single NIOSH survey conducted from 1984 to 1987. There are no available monitoring data from the NIOSH survey prior to 1984. The monitored data from the NIOSH survey represent only 3 years, which is not representative of the SBR cohort exposure from 1944 to 1999. Additionally, no dose-response association was solely dependent on the NIOSH monitored data in previous studies. Therefore, Macaluso 2004 is the most appropriate exposure assessment data. Please see Section 5.4.1.1.2.

4) Excluding the low end of the data range.
The IUR represents a lower exposure range, so excluding the low end of the data range would bias the IUR.

5) Use of BMR 1% versus a much lower level based on power of the study in accordance with EPA BMDS guidance.

i. According to the EPA *Benchmark Dose Technical Guidance* (U.S. EPA, 2012b), 1 percent extra risk is often used as a BMR for epidemiological data, unless the health outcome is a rare cancer. Please see Section 5.4.3.3.
ii. The Surveillance, Epidemiology, and End Results Program (SEER) of the National Cancer Institute indicated that the lifetime risk of bladder cancer is 2.1 percent and leukemia is 1.5 percent. Compared to a much lower level of BMR, such as 0.1 percent or 0.01 percent, a BMR of 1 percent is more appropriate because 1 percent is closer to the lifetime risks of bladder cancer (2.1%) and leukemia (1.5%).

1.5.15.5 Comment

Summary: On pages 131–132, the SACC noted that in the Draft Human Health Hazard Assessment (U.S. EPA, 2024e), Line 2921, Table 7-1 includes this statement, "Elderly people have a higher risk for anemia; however, they should be less susceptible to cancer and reproductive issues than other lifestages." The SACC disagreed noting that, according to the National Cancer Institute, leukemia is more common in older adults. This increased risk and burden is also reflected in the leukemia incidence and mortality data in the lifetable spreadsheet. On page 132 of the SACC report, as a bulleted recommendation, the SACC recommended that EPA consider PESS communities in the lifetime exposure estimates and to give improved attention to and discussion of PESS both with regard to exposure to fenceline communities and sensitive subpopulations.

EPA Response: EPA appreciates this comment and clarifies that the intent of the statement was to acknowledge that that elderly people are less susceptible to developing cancer from future exposures due to less fast-dividing tissues and limited remaining lifetime for cancer to develop. EPA has removed this statement on cancer susceptibility in the elderly from Table 7-1 to reduce confusion. EPA thoroughly discusses all relevant PESS information impacting biological susceptibility in Section 7.2 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d). EPA explains how the risk evaluation incorporated PESS considerations into risk estimates in Section 5.3.5 of the risk evaluation, which includes a breakdown of exposures and cancer risks across demographics.

1.5.15.6 Comment

Summary: As a bulleted recommendation on page 132 of the SACC report, the SACC recommended that EPA should not rely on the Macaluso analysis as the basis for exposure estimates to workers. The SACC noted that this point is further addressed in response to charge question 5.f.i.

EPA Response: See responses to more detailed SACC comments and discussion of the cohort data from Charge Q5f.i in Section 1.5.13 of this document.

1.5.16 Charge Question 5f.iv

On page 132 of the SACC report, the SACC found that the methods used for the derivation of the cancer unit risks are appropriate with some refinements recommended in implementing the lifetable method.

1.5.16.1 Comment

Summary: On pages 134–135 of the SACC report, the SACC noted that the chronic occupational unit risk based on the same life table but without ADAFs is appropriate, but having both unit risk values (occupational and general population) may create confusion. They also noted that clear definitions of each value and term: occupational UR, general population IUR, adult-exposure-based and adult-based unit risks will be helpful (perhaps in a text box in the Draft Human Health Hazard Assessment (U.S. EPA, 2024e)). The general population IUR could be calculated directly using the full lifetable including ages 0–15 and applying the beta coefficient. This was noted as a potentially useful sensitivity analysis. Inconsistencies, such as lifetime assumptions (*e.g.*, 78 or 85 years), were noted by the Committee (and also by public commenters). These were requested to be checked/corrected or explained/justified. Similarly, the SACC recommended that alignments between the EPA lifetable analysis assumptions (*e.g.* durations) should generally align with the occupational exposure assumptions (*e.g.*, consider whether the lifetable for workers should be limited to 40 years from age 16, do not scale the general population IUR from the occupational calculation) a separate lifetable analysis for the general population (full lifetime exposure); *i.e.*, the general population IUR should not be scaled from a 40-year occupational calculation. These inconsistencies also apply to the lifetable for bladder cancer.

EPA Response: The lifetable and IUR are based on the occupational cohort data available as there is not reliable dose-response information from a general population exposure study. However, the derived cancer hazard value is not specific to those workers. The cancer hazard value represents the generalized risk for anyone exposed to 1,3-butadiene under those exposure conditions. Therefore, there is no separate lifetable for different populations as it applies to general population by default and is adjusted for a worker exposure scenario. The final risk evaluation and human health hazard assessment has improved clarification of these terms. Exposure factors (including exposure years) implemented into the lifetable analysis are described in Section 5.3.9.2 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d). The selected parameters represent the best available science considering the reasonably available information while maintaining consistency with EPA guidance and other TSCA risk evaluations. Comparison between assumptions and adjustments incorporated into the exposure and hazard values is provided in Section 5.3.1.3 of the risk evaluation.

1.5.16.2 Comment

Summary: As a bulleted recommendation on page 135 of the SACC report, the SACC recommended that EPA discuss the limited consideration of aggregate exposures and lack of consideration of potential cumulative exposure and risk issues (*e.g.*, exposure to other leukemogens and relevant non-chemical stressors).

EPA Response: See responses from similar comments 1.7.1 and 1.5.15.5.

1.6 Charge Question 6 - Risk Evaluation Transparency, Clarity, Consistency, and Reasonableness

Sections 1.6.1 and 1.6.2 cover general comments on the risk evaluation, associated documents and the risk assessment process. For discipline-specific comments from both Charge Q6a.i and Q6a.ii, see Section 1.6.3.

1.6.1 Charge Question 6a.i

On page 136 of the SACC report, the SACC found that the 1,3-Butadiene Draft Risk Evaluation (U.S. EPA, 2024g) was detailed and generally well-organized and detailed but commented on the characterization and tractability of associated documents.

1.6.1.1 Comment

Summary: As a bulleted recommendation on page 138 of the SACC report, the SACC suggested improving the language and word use throughout the documents. One example is the use of the term "no risk", as absolute terms in risk assessments are neither accurate nor appropriate and risk by definition refers to probability. Risk should not be considered as a binary function – risk is a continuum. Therefore, they recommend considering terms such as "reasonable" or "unreasonable" risk or other similar terms that are not absolute.

Additionally bulleted, SACC noted that descriptions of what data were used and how they were used could be "refined" throughout the documents, to avoid misunderstanding. Commonly used synonyms (assess, review, evaluate, *etc.*) should be mapped to specific tasks and methods and used consistently in a manner appropriate for what was actually done and not used to describe opaque procedures. These could perhaps be defined as part of a technical dictionary.

EPA Response: EPA has removed references to the term "no risk", except in the risk determination context. EPA has also improved clarity and added additional discussion where relevant throughout TSDs and the risk evaluation and will work to better refine word usage and improve consistency generally across future risk evaluations.

1.6.1.2 Comment

Summary: As a bulleted recommendation on page 138 of the SACC report, the SACC recommended EPA to consider an overall Executive Summary that brings together key points and serves as a platform in which each draft report contributes.

EPA Response: EPA has included an executive summary in the draft risk evaluation which summarizes the key points from the various TSDs. This summary has been updated for the final risk evaluation.

1.6.1.3 Comment

Summary: As a bulleted recommendation on page 138 of the SACC report, the SACC recommended that EPA should make the Draft Risk Evaluation Document Map (Figure 2-6) interactive so users could click on map/figure components to go to each document.

EPA Response: EPA will consider making the map interactive in future risk evaluations to allow users to easily navigate to each document by clicking on the map or figure components.

1.6.1.4 Comment

Summary: As a bulleted recommendation on page 139 of the SACC report, the SACC recommended that EPA revise the language and word use in order to provide the reader with an accurate, efficient, road map through the documents, that provides the reader the justification for the steps in the process. The SACC recommended that all TSD summaries should indicate how the TSD informs or fits into the Risk Evaluation overall and links to specific referenced portions of other reports would help the reader.

EPA Response: EPA has included an executive summary in the draft risk evaluation which summarizes the key points from the various TSDs. This summary has been updated for the final risk evaluation. In addition, TSD references are made throughout each document with links, and a document map is included in the beginning of each TSD highlighting how that document connects to others.

1.6.1.5 Comment

Summary: As a bulleted recommendation on page 147 of the SACC report, the SACC recommended that EPA check HERO hyperlinks to ensure that they are correct for the cited study and perform a quality control check to assure that use of the HERO hyperlinks lead to the full documents needed for review. An added bulleted recommendation from SACC requests that study sponsors grant permission for the full original study report to be made available via HERO, or EPA should prepare a more detailed review of these studies.

EPA Response: All studies and data sources used in the risk evaluation were made available for the SACC panel to review through the access-controlled internal HEROnet version of the database. Industry data were submitted in the docket for 1,3-butadiene and is publicly available, however copyrighted data cannot be made freely available to the public. In contrast, the public HERO database serves to provide a public record of what was used in the risk evaluation but is not intended to provide open access to the original data.

1.6.1.6 Comment

Summary: On page 136 of the SACC report, the SACC noted that each report is generally well organized, highly detailed and augmented with supplementary information, and the concluding remarks in the final section of each report are helpful. However, SACC points out the essential need to explain the relevance and importance of the technical information or analysis presented in all documents.

EPA Response: The risk evaluation document integrates all the TSDs into the risk characterization and risk determination. For the final risk evaluation package. All TSDs also now contain a document map highlighting how that document connects to others.

1.6.1.7 Comment

Summary: On page 138 of the SACC report, the SACC recommended that EPA provide a better description of what information is present within databases and what information is relevant including the underlying rationale for creation of the database and collection of the data, specifically to articulate the key items shown by those data. This information should discuss robustness, missing data, what assessments are supported, important variables, and other items of importance to the particular issue (*e.g.*, sources, limitations, use of data and statistical analyses, influencing factors such as timing, environmental factors).

EPA Response: EPA has included additional discussion of databases that were used for the various technical support documents in the 1,3-butadiene risk evaluation. The updates include discussion of robustness, missing data, supported assessments and statistical analyses.

1.6.1.8 Comment

Summary: On page 138 of the SACC report, the SACC recommended that EPA should include a comprehensive discussion of uncertainty used in exposure and effect estimation in the risk assessment to strengthen the analysis and provide information on risk drivers and where data may be less certain. Explaining where assumptions were used and the approximate magnitude of an assumption, allows the reader to follow along, increasing transparency of the assessment, and provides a discussion of how these assumptions can add to the uncertainty of the final risk estimate before concluding "unreasonable risk." Tables can be used to collect this information where semi-quantitative decisions can be made regarding the direction and magnitude of uncertainty (*e.g.* +++ vs + or -, --, etc.). All of the uncertainties should be aggregated.

EPA Response: EPA is continuously improving its approach to defining and characterizing uncertainty and confidence. A semi-quantitative confidence scoring was included in Appendix E of the draft human health risk assessment and detailed explanations for confidence determinations are presented in the other technical support documents as well. The risk evaluation summarizes these conclusions for each discipline and the risk characterization focuses on the uncertainties and confidence in the overall risk conclusions for each scenario and COU.

1.6.2 Charge Question 6a.ii

1.6.2.1 Comment

Summary: On page 146 of the SACC report, as a bulleted recommendation, the SACC recommended that EPA ensure the sponsors provide the full study report for public accessibility. If this does not occur, the EPA should prepare detailed reviews of Hazleton (1981a) and WIL Research (2003) and summarize them more fully in the HHRA and make those summaries accessible via HERO. They also state in another bullet that EPA should perform a quality control check to ensure that use of HERO hyperlinks leads to information useful in the risk evaluation process.

EPA Response: Both of these studies along with all other cited information were available to the SACC panel for review through the HEROnet database. The public version of HERO is restricted to abstract and citation information only due to legal copyright requirements, however the SACC received login information and instructions for accessing copyrighted studies for review. Hyperlinks are only available for public documents/references and these links are always subject to change, however the citation information will remain accurate for the public while peer reviewers can access the studies through the restricted login. See also response to comment 1.6.1.1. In addition, please see the *Data Quality Evaluation Information for Human Health Hazard Animal Toxicology for 1,3-Butadiene* (U.S. EPA, 2025n), *Data Quality Evaluation Information for Human Health Hazard Epidemiology for 1,3-Butadiene* (U.S. EPA, 2025o), and *Data Extraction Information for Human Health Hazard Animal Toxicology and Epidemiology for 1,3-Butadiene* (U.S. EPA, 2025a) for details on animal toxicology and epidemiology studies.

1.6.2.2 Comment

Summary: On page 153 of the SACC report, in as a bulleted recommendation on page 153 of the SACC report, the SACC recommended that EPA should use tables and visuals to cement the key points and enhance the reader's comprehension; refer to an example in Section 4 of the Risk Assessment Handbook.

EPA Response: EPA has made efforts to incorporate readability and user-enhancement improvements within the constraints of time and resources to meet our deadlines. EPA will continue to strive for clarity and effectiveness in our documents.

1.6.2.3 Comment

Summary: A bulleted recommendation on page 153 of the SACC report noted that if there are specific documents or sections within a document, EPA should identify that section or provide the relevant link to the specific section in the technical support documents. Having only a reference to a full report is not very useful.

EPA Response: TSD references are made throughout each document with links. EPA is considering modifications to the risk evaluation package for future chemical assessments to reduce the number of total documents while still keeping the technical reports distinct from the risk characterization. By combining related technical sections into the same document, it will be easier to provide specific cross-links to the relevant sections.

1.6.2.4 Comment

Summary: In a bulleted comment on page 153 of the SACC report, the SACC recommended that EPA include a problem formulation statement within the risk evaluation documents. They noted that a problem formulation could describe the manner in which the draft risk evaluation considers previously identified important elements, including toxic transformation products of 1,3-butadiene, aggregate exposures, PESS, cumulative exposures to non-chemical stressors.

EPA Response: EPA plans to incorporate problem formulations into the scope documents for future TSCA risk evaluations.

1.6.2.5 Comment

Summary: The SACC recommended in a bullet on page 153 of their report that EPA develop a technical dictionary for commonly used terms. Consistent and clear language and word use will assist readers and offer justification for the steps in the process.

EPA Response: The definitions and use of these words have varying contexts across disciplines and risk assessment contexts. EPA is always striving to improve consistency within and across risk evaluations and will consider defining these terms in a future glossary or dictionary. See also response to comment 1.6.1.1.

1.6.2.6 Comment

Summary: SACC recommended in a bulleted comment on page 153 of their report that EPA develop a broader "vision" of the continuum from Manufacturing to Disposal to fully understand worker, general population and PESS exposure opportunities. They also recommended the inclusion of a “grand” compilation of uncertainties across the components of the assessment, suggesting that a more-thorough uncertainty assessment may also highlight specific gaps and limitations of the assessment that should also be summarized so that subsequent assessments can be improved.

EPA Response: EPA is continuously striving to improve the integration of exposures and risks along the life cycle of a chemical while still following the guidelines of the statute and risk evaluation rule. This includes capturing and discussing uncertainties from each aspect of the evaluation in an integrated manner. EPA will continue to expand the depth and utility of uncertainty assessments in future risk evaluations.

1.6.2.7 Comment

Summary: The SACC recommended in a bullet on page 154 of their report that EPA prepare a "summary of summaries" document encompassing the TSDs. This can be a compilation of the summary pages from each TSD – so the key points of all TSDs can be found together. This would reduce the need to search for the separate TSDs. EPA should also revise the approach to organization/presentation. If possible, make the Draft Risk Evaluation Document Map (Figure 2-6) interactive so users could click on map/figure components to go to each document.

EPA Response: The risk evaluation document serves as a "summary of summaries", as it includes the executive summary which summarizes the key points from the various TSDs and key tables from each TSD. As mentioned above, EPA is considering modifications to the risk evaluation package for future chemical assessments. EPA will also work to implement an interactive document map, where possible.

1.6.2.8 Comment

Comment: The SACC suggested in a bulleted recommendation on page 154 of their report that t that the non-technical, public summary of the Risk Evaluation should include a description of the process for generating documents and conclusions, including internal and external reviews.

EPA Response: EPA is continuously improving the non-technical summary to better achieve the task of presenting the important conclusions of the risk evaluation for the public.

1.6.3 Discipline-Specific Comments

These comments were generally listed as bullets across charge questions 6a.i and 6a.ii, with some important points not covered by bullets also summarized.

1.6.3.1 Physical-Chemistry and Fate Assessment

1.6.3.1.1 Comment

Summary: On page 139 of the SACC report, the SACC recommended, as a bullet in their report, that the summary of the fate TSD should indicate that fate estimates are based on modeling. They state that the summary should also explain what happens next, *i.e.*, a qualitative/descriptive assessment was developed.

EPA Response: Revisions have been made to the summary of the *Physical Chemistry, Fate, and Transport Assessment for 1,3-Butadiene* (U.S. EPA, 2025f) to indicate its support for qualitative assessments of environmental exposure to 1,3-butadiene in water, sediments, and soil in addition to oral exposure to 1,3-butadiene for the general population, and dermal exposure for workers and consumers. EPA notes however that fate assessments are based on both measured and modeled data, not just modeled data. Table 2-1 and 3-1 in the *Physical Chemistry, Fate, and Transport Assessment for 1,3-Butadiene* (U.S. EPA, 2025f) notes which fate properties are based on measured data and which ones are based on modeled data.

1.6.3.1.2 Comment

Summary: The SACC suggested in a bulleted recommendation on page 139 of their report that the summary of Section 3.4.2 of the *Physical Chemistry, Fate, and Transport Assessment for 1,3-Butadiene* (U.S. EPA, 2025f) should describe the underlying evidence concisely. For example: "The data were gathered and evaluated as part of the systematic review process. The physical chemistry and fate

assessment data reported and applied in the risk evaluation come from experimental studies and government documents." (As presented in Table 2-1.)

EPA Response: A description of the underlying evidence for the fate assessment is documented in Section 2.0 of the *Physical Chemistry, Fate, and Transport Assessment for 1,3-Butadiene* (U.S. EPA, 2025f).

1.6.3.1.3 Comment

Summary: The SACC suggested in a bulleted recommendation on page 140 of their report that the description of solubility in aquatic systems should be augmented to include the likelihood of 1,3-butadiene occurrence and any information about measured presence, so the reader puts the physical characteristics into the context of potential for exposure.

EPA Response: Edits have been made to Section 3.5.2 of the *Physical Chemistry, Fate, and Transport Assessment for 1,3-Butadiene* (U.S. EPA, 2025f) as suggested.

1.6.3.1.4 Comment

Summary: The SACC suggested in a bulleted recommendation on page 140 of their report that EPA should estimate the proportion of 1,3-butadiene that would be released into the environment and photodegraded (see Charge Question 1.a.). They state that the point is important in understanding the potential risk from formaldehyde and acrolein in the environment.

EPA Response: This information was documented in Section 3.4.2 of the *Draft Physical Chemistry, Fate, and Transport Assessment for 1,3-Butadiene* (U.S. EPA, 2024f).

1.6.3.1.5 Comment

Summary: The SACC suggested in a bulleted recommendation on page 140 of their report that the EPA include a sentence outlining the criteria for data quality ratings, ensuring that readers are informed about the comprehensive review process applied to all references included in the risk evaluation.

EPA Response: Edits have been made to Section 1.2 of the *Physical Chemistry, Fate, and Transport Assessment for 1,3-Butadiene* (U.S. EPA, 2025f). as suggested. For more details see the *Systematic Review Protocol for 1,3-Butadiene* (U.S. EPA, 2025h).

1.6.3.2 Environmental Media Concentrations

1.6.3.2.1 Comment

Summary: The SACC suggested in a bulleted recommendation on page 141 of their report that EPA report all 1,3-butadiene concentrations in air as $\mu g/m^3$.

EPA Response: All 1,3-butadiene concentrations in air have been written/reported in $\mu g/m^3$ in both text and figures where possible. For figures that report in ppm or ppb, the conversion to $\mu g/m^3$ is provided in text.

1.6.3.2.2 Comment

Summary: The SACC suggested in a bulleted recommendation on page 140 of their report that EPA label the columns of the Excel document (in Section 3.1.2 Monitoring Database of the *Draft Ambient*

Monitoring Technology Information Center (AMTIC) Monitoring Data 310 *2016 to 2021 for 1,3-Butadiene* (U.S. EPA, 2024c)) that contain AMTIC data.

EPA Response: All columns in supplemental file have been labeled.

1.6.3.2.3 Comment

Summary: The SACC suggested in a bulleted recommendation on page 140 of their report that EPA provide language to note that Texas data goes through 3/31/21 and not through the end of 2021. This may be needed for other states as well.

EPA Response: EPA redownloaded all AMTIC data 2016–2022 and ensured that all months in 2021 and 2022 are included, as well as Texas and Louisiana data.

1.6.3.2.4 Comment

Summary: The SACC suggested in a bulleted recommendation on page 140 of their report that Section 5.1 should describe the extent of measured concentrations data for groundwater in WQP, to resolve uncertainties about 1,3-butadiene in groundwater as discussed earlier in charge question 2.

EPA Response: Section 5.1 of the *Environmental Media Concentrations for 1,3-Butadiene* (U.S. EPA, 2025b) has been updated to include more discussion of the limitations of the groundwater data

1.6.3.2.5 Comment

Summary: The SACC suggested in a bulleted recommendation on page 141 of their report that for future assessments, EPA should determine if the WQP data are of high enough quality to be in risk evaluation documents.

EPA Response: The WQP was used in the 1,3-butadiene risk evaluation as it represents a comprehensive, publicly available data repository that aggregates water quality data from multiple reliable sources (*e.g.* USGS, EPA STORET and state agencies). The WQP is generally recognized as a reliable source of environmental monitoring information. EPA will continue to ensure that only high-quality data are incorporated into risk evaluation documents.

1.6.3.2.6 Comment

Summary: The SACC suggested in a bulleted recommendation on page 141 of their report that EPA include some discussion of the number of non-detects (and reporting limits) in Table Apx C-1 (Summary of AMTIC Monitoring Data 2016–2021 for 1,3-Butadiene).

EPA Response: Number and percentage of non-detects and ranges for method detection limits and reporting limits are provided in context for both 24-hour cannister samples and 1-hour Auto-GC samples.

1.6.3.2.7 Comment

Summary: SACC suggested in a bulleted recommendation on page 141 of their report that EPA provide a more robust explanation about the information to be gained in a qualitative assessment. In another bulleted recommendation on the same page, they requested EPA define gray literature (Line 249).

EPA Response: A qualitative assessment allows inferences to be made about the likelihood of exposures or presence of the chemical in the environment in the absence of available measured data.

EPA has added the definition of gray literature in Section 2 Approach and Methodology of the *General Population Exposure Assessment for 1,3-Butadiene* technical support document (U.S. EPA, 2025c).

1.6.3.3 General Population Exposures

1.6.3.3.1 Comment

Summary: SACC recommended on page 141 of their report that that EPA check the accuracy of all figures and tables in the *General Population Exposure Assessment for 1,3-Butadiene* technical support document (U.S. EPA, 2025c).

EPA Response: Figures and tables have been checked for accuracy.

1.6.3.3.2 Comment

Summary: SACC recommended on page 141 of their report that EPA include more details about AirToxScreen including how the maximum predicted ambient concentration in Region 7 fits with modeled data.

EPA Response: AirToxScreen is assessment conducted by the Office of Air and Radiation (OAR) and not the Office of Pollution Prevention and Toxics (OPPT) that serves as a screening tool based on modeling of NEI release data. EPA acknowledged, provided an overview and referenced the AirToxScreen as means to help contextualize other sources of 1,3-butadiene and their contribution to ambient air concentrations in Section 2.3.2.2 of the *General Population Exposure for 1,3-Butadiene* (U.S. EPA, 2025c).

1.6.3.3.3 Comment

Summary: SACC suggested on page 142 of their report that the figure depicting 1,3-Butadiene Ambient Air Concentrations and Non-combustion Sources from AirToxScreen 2020 could be made easier to read and understand.

EPA Response: For the *Draft General Population Exposure for 1,3-Butadiene* technical support document (TSD) (U.S. EPA, 2024d), two separate figures (Figure 2-3 and 2-4) were created, one to illustrate source categories related to fuel use and combustion (mobile emissions, residential wood burning, natural fires, etc.) and the other to illustrate source categories not related to fuel use and combustion (stationary sources, residential and commercial lawn and equipment, etc.) and their relative contributions to modeled 1,3-butadiene ambient air concentrations. These two figures remain unchanged in the final *General Population Exposure for 1,3-Butadiene* TSD (U.S. EPA, 2025c) because EPA maintains that this was the best way to illustrate these source categories based on the AirToxScreen assessment conducted by OAR using NEI 2020 release data.

1.6.3.4 Environmental Release and Occupational Exposure Assessment

1.6.3.4.1 Comment

Summary: SACC suggested in a bulleted recommendation on page 143 of their report that EPA should provide a figure or flow chart showing how the data, the multiple models and their predictions (IIOAC modeling, HEM modeling, NEI evaluation, monitoring data, and AirToxScreen) fit together to yield the determination of risk from 1,3-butadiene.

EPA Response: A figure comparing IIOAC TRI, HEM TRI and HEM NEI modeled concentrations and AMTIC 24-hour and 1-hour concentrations was added in Section 2.3.1.1 of the *General Population Exposure for 1,3-Butadiene* technical support document (U.S. EPA, 2025c).

1.6.3.4.2 Comment

Summary: SACC suggested in a bulleted recommendation on page 143 of their report that EPA should state in the text of the *General Population Exposure Assessment for 1,3-Butadiene* TSD (U.S. EPA, 2025c) that the use of the 95th percentile of concentrations of 1,3-butadiene may underestimate the exposure and associated risk for PESS communities. There was also a bulleted recommendation on the same page to state that the selected concentrations may underestimate the actual concentrations due to environmental factors. Alternatively, the EPA should conduct a probabilistic analysis of the concentrations and discuss the impacts of the higher concentrations on PESS.

EPA Response: The use of the 95th percentile of modeled concentrations of 1,3-butadiene along with the assumption that exposure is occurring continuously for 24 hours day, 365 days a year over a lifetime in conjunction with the general population IUR that considers PESS factors by including an Age Dependent Adjustment Factor (ADAF) is more likely to overestimate exposure and associated risk estimates.

1.6.3.4.3 Comment

Summary: SACC suggested on page 137 of their report that that EPA consider the effects that documented night-time pulsed released of 1,3-butadiene to the air have on half-life predictions, modeled concentrations, and distances needed to capture exposures.

EPA Response: The AERMOD Gaussian plume dispersion within the models does not have the capability to take secondary air pollutant formation under consideration. Therefore, EPA is not able to consider or discuss differences in concentrations during overnight hours or during daylight hours. However, the integration of urban/rural populations within the models used is designed to consider effects like heat islands which can cause higher concentrations over nighttime hours. Since the estimates from the models do not assume that 1,3-butadiene is being photo oxidized or transforming into other chemicals in the air during daylight hours and stays as 1,3-butadiene, the modeled concentrations from both IIOAC and HEM would be conservative estimates.

1.6.3.4.4 Comment

Summary: SACC recommended on page 141 of their report that EPA check all figures and tables for accuracy in the *Environmental Release and Occupational Exposure Assessment* (U.S. EPA, 2025p).

EPA Response: Figures and tables have been checked for accuracy.

1.6.3.5 Human Health Hazard

1.6.3.5.1 Comment

Summary: SACC suggested in a bulleted recommendation, on page 145 of the SACC report, that EPA improve the discussion so that all cited studies rise to level of the Battelle PNL (1987) study, providing sufficient information in a succinct presentation. EPA should improve the level of detail in the study descriptions to provide sufficient documentation and integrated narrative.

EPA Response: The study summaries match the complexity and number of results for that study. The Battelle study (1987) was the most important study for gestational effects, which was the basis of the POD used for risk estimates. It was not discussed at all in the hazard identification summary for male reproductive and hematological effects, where other key studies were the focus of the discussion for this critical health outcomes. Additional details from every study considered are provided in the systematic review supplemental documents, which include an extraction of all endpoints assessed in the key studies. The database for each major health outcome along with a formal evaluation of the weight of scientific evidence is also presented in the evidence integration tables in Appendix A of the human health hazard assessment.

1.6.3.5.2 Comment

Summary: SACC requests on page 145 of their report that that study sponsors grant permission for the full original study report to be made available via HERO, or alternatively EPA should prepare detailed reviews. The SACC also requests in a bulleted recommendation, on page 147 of the SACC report, that the EPA, in collaboration with the HERO manager, conduct a quality control check to ensure that HERO hyperlinks direct users to the full documents required for review.

EPA Response: See response to similar comment in Section 1.6.1.5.

1.6.3.5.3 Comment

Summary: SACC recommended on page 144 of their report, that EPA clarify what "guideline-like" means in the *Draft Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2024e).

EPA Response: EPA has added clarification to the final *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d) for the meaning of this term. "Guideline-like" means that the study did not formally follow a guideline, but the methods and level of detail presented are highly similar to current OECD guideline requirements.

1.7 Other Topics Not Covered by Charge Questions

1.7.1 Comment

Summary: The SACC noted on page 148 of their report, that there are gaps in fully understanding exposure opportunities along the continuum of manufacturing of the chemical, use in other manufacturing, processing, re-packaging, distribution, transportation, *etc*. In a bolded recommendation, SACC stated that there is a need for inclusion of additional exposure opportunities within these TSCA Existing Chemical assessments. Other gaps include absence of consideration of fracking, disposal, public spaces (malls, offices, retail, schools, *etc*.). In a bolded recommendation, the SACC stated that quantitative studies of off-gassing, polymerization efficiency or other tested and substantiated data should be considered. They recommend that EPA should also consider aggregate and cumulative exposure and the use of distributions of values for exposure assessment and algorithm parameters, even as a source of background exposure. There is a lack of consideration of potential cumulative exposure and risk issues (*e.g.*, exposure to other leukemogens and relevant non-chemical stressors).

EPA Response: EPA agrees that there is imperfect knowledge of all potential releases and exposures that may occur throughout the life cycle of a chemical such as 1,3-butadiene. EPA considers all reasonably available information to inform the risk evaluation. As to specific examples mentioned in the comment, EPA has determined that 1,3-butadiene is not present in any fracking materials, while it is unclear what sources would be present in public spaces other than combustion sources, which was not

assessed as an independent COU subcategory in this risk evaluation. Polymerization and disposal of 1,3-butadiene were included as occupational conditions of use and exposure scenarios, and for the final risk evaluation EPA added a quantitative consumer assessment of risk from 1,3-butadiene off-gassing from children's toys. The impact of other chemicals is outside of the scope of the risk evaluation for 1,3-butadiene. The purpose of the risk evaluation under TSCA is to determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, under the conditions of use.

1.7.2 Comment

Summary: The SACC stated on page 160 of their report, that EPA only uses deterministic models without considering data distributions. In contrast, probabilistic models utilize curve fitting for use of parametric and non-parametric distributions, eliminating the need to choose a single value within the distribution. Aggregate exposure to an individual requires modeling the probability and time-related repetition of exposures. Therefore, in a bulleted statement the SACC Committee strongly recommends that the EPA leadership provide the resources and support that their scientists need to create or adopt methods and models which provide competent aggregate exposure assessments and comprehensive analysis options to assess the relevance and effectiveness of different risk mitigation options.

EPA Response: EPA considered the use of models; however, EPA did not find models that were suitable for 1,3-butadiene and had monitoring data to use for each OES. However, EPA will consider incorporating more probabilistic modeling into future risk evaluations under TSCA.

1.7.3 Comment

Summary: On page 163 of the SACC report, the SACC had the following general concerns about the selection of the references: The systematic epidemiologic literature review omitted details on study design, a major criterion for inclusion of any paper. Consequently, the papers were not subjected to a complete critical analysis of how the study design might have introduced bias, allowing conclusions that are not consistent with a well-conducted systematic review. The review did not discuss potential for conflict of interest. A way to statistically deal with the healthy worker effect is to consider internal comparisons within the same cohort population (see Chowdhury et al., 2017). This has the additional advantage of allowing for further data collection and analysis. The Johns Hopkins cohort researchers attempted a nested case-control study design that helped in more accurate validation of the pathology diagnosis, identifying the cases in underlying and contributory causes, and gaining more precision in the work histories. With this design, it was possible to identify the risk ratio for leukemia with greater precision, first with a matched design (Santos-Burgoa et. al, 1992), and later with unmatched and with the use of monitoring data, where available (Matanoski et al., 1997).

EPA Response: In the EPA systematic review for the epidemiological studies (U.S. EPA, 2021), "Analysis" is one of the evaluation criteria in the evaluation form, and it assesses the study design and method, reproducibility of analysis, and statistical models. In addition, Section 5.3.7.3 of the Human Health Hazard Assessment compares the study design, and statistical modeling among the publications of the SBR cohort study and other ecological and case-control studies to select the best study for IUR derivation. The best study and model that was selected for the IUR derivation used internal controls, as the comment suggests (Chowdhury et al., 2017).

1.7.4 Comment

Summary: On page 163 of the SACC report, the SACC requested that EPA has considered the following references:

- Matanoski, G., Elliott, E., Tao, X., Francis, M., Correa-Villasenor, A., & Santos-Burgoa, C. (1997). Lymphohematopoietic cancers and butadiene and styrene exposure in synthetic rubber manufacture. *Annals of the New York Academy of Sciences*, *837*, 157–169. https://doi.org/10.1111/j.1749-6632.1997.tb56872.x
- Matanoski, G., Francis, M., Correa-Villaseñor, A., Elliott, E., Santos-Burgoa, C., & Schwartz, L. (1993). Cancer epidemiology among styrene-butadiene rubber workers. *IARC Scientific Publications*, *127*, 363–374.
- Matanoski, G. M., Santos-Burgoa, C., & Schwartz, L. (1990). Mortality of a cohort of workers in the styrene-butadiene polymer manufacturing industry (1943-1982). *Environmental Health Perspectives*, *86*, 107–117. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1567763/
- Matanoski GM, Schwartz L. Mortality of workers in styrene-butadiene polymer production. J Occup Med. 1987 Aug;29(8):675-80.
- Santos-Burgoa C. P. Case-control study of lympho-hemopoietic malignant neoplasms within a cohort of styrene-butadiene polymerization workers. (1988). Johns Hopkins University. Dissertation Number 8908149. https://www.proquest.com/dissertationstheses/case-control-study-lympho-hemopoietic-malignant/docview/303705487/se-2?accountid=11243
- Meinhardt, T. J., Lemen, R. A., Crandall, M. S., & Young, R. J. (1982). Environmental epidemiologic investigation of the styrene-butadiene rubber industry. Mortality patterns with discussion of the hematopoietic and lymphatic malignancies. *Scandinavian Journal of Work, Environment & Health*, *8*(4), 250–259. https://doi.org/10.5271/sjweh.2469
- Meinhardt, T. J., Young, R. J., & Hartle, R. W. (1978). Epidemiologic investigations of styrene-butadiene rubber production and reinforced plastics production. *Scandinavian Journal of Work, Environment & Health*, *4 Suppl 2*, 240–246.

EPA Response: The EPA systematic review process included these studies for consideration.

2 Public Comments Posted on EPA-HQ-OPPT-2018-0451

1,3-Butatdiene public comments on the docket numbered EPA-HQ-OPPT-2018-0451 are summarized in the subsections below.

Table 2-1. Index of Public Comment Submissions to Docket EPA-HQ-OPPT-2018-0451, Sorted by Submission Number

Submission Number	Commenter Name
EPA-HQ-OPPT-2018-0451-0046	Sarah Amick/U.S. Tire Manufacturers Association (USTMA)
EPA-HQ-OPPT-2018-0451-0049	Earthjustice et al.
EPA-HQ-OPPT-2018-0451-0050	Katherine O'Brien/Earthjustice
EPA-HQ-OPPT-2018-0451-0051	Earthjustice et al.
EPA-HQ-OPPT-2018-0451-0052	Neeraja Erraguntla/American Chemistry Council (ACC)
EPA-HQ-OPPT-2018-0451-0053	American Chemistry Council (ACC)
EPA-HQ-OPPT-2018-0451-0054	Ivan Rusyn
EPA-HQ-OPPT-2018-0451-0056	Kat Gale/American Chemistry Council (ACC)
EPA-HQ-OPPT-2018-0451-0057	Environmental Defense Fund (EDF)
EPA-HQ-OPPT-2018-0451-0058	Suzanne Hartigan/American Chemistry Council (ACC)
EPA-HQ-OPPT-2018-0451-0059	Washington State Departments of Ecology and Health
EPA-HQ-OPPT-2018-0451-0060	Environmental Defense Fund (EDF)
EPA-HQ-OPPT-2018-0451-0063	Rebecca O'Donnell/American Chemistry Council (ACC)
EPA-HQ-OPPT-2018-0451-0064	Suzanne Hartigan/American Chemistry Council (ACC)
EPA-HQ-OPPT-2018-0451-0067	Suzanne Hartigan/American Chemistry Council (ACC)
EPA-HQ-OPPT-2018-0451-0068	Janelle Reese/INV Nylon Chemicals Americas, LLC

2.1 General

2.1.1 Comment

Summary: One public commenter (EPA-HQ-OPPT-2018-0451-0046) requested that EPA extend the public comment period for 1,3-butadiene in 2020, expressed an interest in working with EPA to provide information needed for risk evaluation, supported the conditions of use outlined in the *Draft Scope of the Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2020a), provided information on residual 1,3-butadiene monomer in butadiene rubber, and made assertions about exposures to 1,3-butadiene. The comment's statements on exposure included general comments on exposure assessment approaches; information on occupational exposure and manufacturers' efforts to limit exposure to 1,3-butadiene; recommendations and information related to occupational, general population, and environmental exposures; and recommendations against using information from the Occupational Safety and Health Administration (OSHA), National Institute for Occupational Safety and Health (NIOSH), and OECD Emission Scenario documents due to concerns about the age and representativeness of the information. Further, the comment recommended that EPA exclude uses that are regulated under other statutes from the scope of the risk evaluation and recommended against using styrene as an analogue to fill data gaps on residual monomer in polymers. The recommendation concluded that water is not a significant pathway for 1,3-

butadiene exposure due to its volatility and low detection in drinking water samples, and further suggested that 1,3-butadiene is unlikely to be present in biosolids or sediments because it predominantly partitions to the atmosphere and does not significantly adsorb to soil or sediment, negating the need for EPA to evaluate its impact in these media.

EPA response: The docket for 1,3-butadiene was open for much of December 2020 through July 2024. Through multiple sources of information described in the *Risk Evaluation for 1,3-Butadiene* Section 4.1.1.1, Section 5.1.2, and Appendix E.9 (U.S. EPA, 2025g), EPA determined that residual 1,3-butadiene monomer in rubber and other polymers is of sufficiently low concentration to be excluded from the risk evaluation. In conducting its exposure assessments, EPA selected exposure scenarios that are representative of real-world behaviors using sources such as the *Exposure Factors Handbook.* Occupational exposure information was provided in comment EPA-HQ-OPPT-2018-0451-0037, and was considered and incorporated into Section 3.6.4 of the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene* (U.S. EPA, 2025p). At the time of drafting, EPA policy was to generally include all conditions of use that are within the jurisdiction of TSCA; thus, those uses that are regulated under other statutes from the scope of the risk evaluation were not excluded. For the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g), EPA did not use styrene as an analogue to fill data gaps on residual monomer in polymers, nor did EPA assess water and biosolids as significant exposure pathways. Information collected through systematic review was considered regardless of its age, and whether and how the information was used in the risk evaluation was based on its relevance and representativeness to current practices.

2.1.2 Comment

Summary: A public commenter (EPA-HQ-OPPT-2018-0451-0049) recommended that the Agency gain additional data for TSCA High Priority Substances including 1,3-butadiene. The recommendations relevant to 1,3-butadiene included using EPA's testing authority under TSCA section 4 to obtain data on hazards and releases; using its authorities under TSCA sections 4, 8, and 10 to obtain information on non-TSCA conditions of use; requiring submission of unpublished data under the Health and Safety Data Reporting Rule; and requiring Preliminary Assessment Information Reporting from facilities. This duplicates a comment entered in another docket, EPA-HQ-OPPT-2020-0473.

EPA Response: EPA did not identify gaps in data required to complete the 1,3-butadiene risk assessment that necessitated the use of TSCA section 4 testing authorities. The Agency reviewed data submissions through TSCA sections 4, 5, 8(a), 8(d), and 8(e) as part of its routine systematic review process for existing chemicals assessments. Non-TSCA conditions of use were identified through review of reported uses, interactions with stakeholders, and review of available information such as Safety Data Sheets. Non-TSCA conditions of use are out of the scope of the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g). EPA required submission of data through a section 8(d) Health and Safety Data Reporting Rule, finalized in June 2021 (86 FR 34147). EPA did not exercise its authority to require reporting under the Preliminary Assessment Information Reporting rule for 1,3-butadiene as the existing data were deemed sufficient to address the scope of the 1,3-butadiene risk evaluation.

2.1.3 Comment

Summary: One public commenter (EPA-HQ-OPPT-2018-0451-0051) proposed that the Agency for Toxic Substances and Disease Registry (ATSDR) develop Toxicological Profiles for TSCA Work Plan chemicals including 1,3-butadiene. This duplicates a comment made in the ATSDR docket (ATSDR-2021-0006) and additionally suggests that EPA collaborate with ATSDR on methodologies for conducting cumulative risk assessments under TSCA.

EPA Response: ATSDR is independent from EPA and EPA does not control ATSDR's process for selecting substances for Toxicological Profiles. The Toxic Substances Control Act statute does not require EPA to conduct cumulative risk assessments, although the Agency may complete cumulative assessments on a chemical-specific basis when the best available science indicates that it is an appropriate course. The approaches to be taken in such a cumulative risk evaluation are dependent on the endpoints to be assessed and the information available for the chemicals included in the assessment.

2.1.4 Comment

Summary: Several comments (EPA-HQ-OPPT-2018-0451-0056, 0058, 0064, and 0067) requested that the public comment periods be extended.

EPA Response: Three requests (0056, 0058, 0064) were granted, with the relevant public comment periods either extended or reopened shortly after closing. One comment was not granted (0067). Comment 0067 was responding to the EPA January 11, 2024, Notice Memo to Re-Open Regulations.gov dockets for 17 High-Priority Substances and for a Manufacturer Requested Risk Evaluation and requested that the public comment period to provide the public an opportunity to submit information to inform the risk evaluation scheduled to close on July 18, 2024, be extended to a deadline of January 18, 2025. The public comment period for the *Draft Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2024g) opened on December 3, 2024, after its publication. This public comment period was originally scheduled to close on February 3, 2025, and was extended to March 5, 2025, because EPA released a supplement to the draft risk evaluation for 1,3-butadiene to give ample time for public comment and peer review. The supplement refines the cancer risk estimates from exposure to 1,3-butadiene in air from releasing facilities

2.1.5 Comment

Summary: One commenter (EPA-HQ-OPPT-2018-0451-0059) submitted primary data, authoritative government reports, a non-exhaustive summary of current regulations and restrictions, and recommendations for EPA's consideration in the risk evaluation process for 1,3-butadiene and other High Priority Substances. The only information source that the comment indicated for 1,3-butadiene was the State of Washington's Environmental Information Management System (EIMS).

EPA Response: EPA relied on national-scale databases such as the Ambient Monitoring Technology Information Center's (AMTIC) database on ambient air monitoring data and the Water Quality Portal (WQP) for surface water monitoring data (Sections 3 through 5 of the *Environmental Media Concentrations for 1,3-Butadiene* (U.S. EPA, 2025b)) which also contained samples from the state of Washington. EPA also reviewed the state of Washington's EIMS, which contains sample concentrations collected during site investigations and remediations, and the data were within the range of the monitored data already available in the national scale databases. All water samples in the EIMS database were reported as non-detects/below the limit of detection (LOD). Section 5.1 and 6.2 of the *Environmental Media Concentrations for 1,3-Butadiene* (U.S. EPA, 2025b) has been updated with this information.

2.2 Occupational Exposure

2.2.1 Comment

Summary: A commenter (EPA-HQ-OPPT-2018-0451-0068) described industrial practices at a site operated by INV Nylon Chemicals Americas, LLC, including uses, occupational exposures, and environmental controls.

EPA Response: This information was considered and incorporated into the process description and occupational exposure sections for the OES of Repackaging (Section 3.2) and Processing as a reactant (Section 3.3) in the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene* (U.S. EPA, 2025p).

2.2.2 Comment

Summary: A public commenter (EPA-HQ-OPPT-2018-0451-0063) submitted information on a literature review including keyword searching and document screening and tagging, to investigate the impact of workplace training and certification programs on occupational health and safety. The analysis identified 56 studies that compared workplaces with safety training programs to those without, and reports that 52 of those 56 studies found a positive benefit (*i.e.*, improved safety) in workplaces with training programs.

EPA Response: This information will be used to inform consideration of risk management options, in the phase following publication of the final risk evaluation.

2.2.3 Comment

Summary: One commenter (duplicate submission as EPA-HQ-OPPT-2018-0451-0052 and 0053) submitted an industrial hygiene data report titled *Analysis of 1,3-Butadiene Industrial Hygiene Data*. This report includes a compilation, and analyses of existing personal breathing zone (PBZ) air concentration samples collected between the years of 2010 and 2019 at 47 facilities that manufacture and process 1,3-butadiene. Full-shift inhalation samples representing eight job groups were included, and short-term and task-based inhalation samples from five tasks.

EPA Response: This information was incorporated into Section 3 of the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene*, where it was used to assess seven occupational exposure scenarios (OESs) (See Table 5-1 of the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene* (U.S. EPA, 2025p)). Worker activities information from the study was used in Section 3.1.4.1 of the same document, and PPE information from the study was used in Section 5.3.2.1 of the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g).

2.2.4 Comment

Summary: One commenter (EPA-HQ-OPPT-2018-0451-0069) submitted a study summary with evidence that residual 1,3-butadiene may not be present above trace amounts in Nylon 66. Because a standard sample of 1,3-butadiene was not available, the study used gas chromatography with mass spectrometry (GC-MS) in selected-ion monitoring (SIM) mode to detect the ions expected to form from 1,3-butadiene.

EPA Response: The provided data support EPA's conclusion that, based on multiple lines of evidence, residual concentrations of 1,3-butadiene in polymers are very low, and often not detectable. Although EPA determined that there is limited potential for exposure to residual 1,3-butadiene monomer in products made from 1,3-butadiene polymers, EPA conducted a sensitivity analysis for exposure and risk estimates in toys using the Consumer Exposure Model (CEM; *Risk Evaluation for 1,3-Butadiene* Section 5.3.3 (U.S. EPA, 2025g)). CEM modeling was conducted for residual 1,3-butadiene up to 30% by weight in 4 m^2 surface area, and the results did not indicate potential risks to infants (the most sensitive population).

2.3 Human Health Hazard Assessment (Non-Cancer/Overall)

2.3.1 Comment

Summary: One commenter (EPA-HQ-OPPT-2018-0451-0054) submitted a peer-reviewed publication by Erber et al. (2021) on estimated variability of formation of 1,3-butadiene DNA adducts.

EPA Response: The human health hazard assessment for 1,3-butadiene considers metabolite adducts in the understanding of species and sex-specificity of metabolism. This study has been added to the final human health hazard assessment to inform the discussion of metabolism, species differences, and consideration of data derived extrapolation factors.

2.4 Potentially Exposed or Susceptible Subpopulations (PESS)

2.4.1 Comment

Summary: A public commenter (EPA-HQ-OPPT-2018-0451-0050) requested that EPA assess fenceline communities as PESS, conduct cumulative risk assessments across chemicals that fenceline communities are exposed to, and to expand the types and amount of information collected under the Chemical Data Reporting (CDR) rule and the Toxics Release Inventory (TRI).

EPA Response: EPA assessed exposures to populations in fenceline communities and other PESS groups as described in Sections 5.3.4, 5.3.5, and 7.1.5 of the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g). The Toxic Substances Control Act statute does not require EPA to conduct cumulative risk assessments, although the Agency may complete cumulative assessments on a chemical-specific basis when the best available science indicates that it is an appropriate course. At this time EPA is not performing a cumulative risk assessment for 1,3-butadiene. The Agency notes that a *Draft Proposed Approach for Consideration of Chemical Co-exposure in TSCA Risk Evaluations* was published and peer-reviewed in 2024 and may inform future risk evaluations (U.S. EPA, 2024b).

EPA updates the information collected under CDR and TRI periodically through rulemaking and comments on those efforts can be submitted to EPA via the docket for those actions at regulations.gov. In addition, two separate petition processes exist for making amendments to CDR (for more information, see https://www.epa.gov/chemical-data-reporting/cdr-petitions).

2.4.2 Comment

Summary: A commenter (EPA-HQ-OPPT-2018-0451-0057) provided information on PESS for 1,3-butadiene, including exposure in fenceline communities, biomonitoring data, and biological susceptibility. The information about fenceline communities included air and water releases and data on accidental chemical releases. The biomonitoring information focuses on concentrations of 1,3-butadiene urinary metabolites in cigarette smokers. Information on biological susceptibility was centered on the potential for genetic polymorphism in metabolic enzymes to impact toxicokinetics and thus increase susceptibility to the effects of 1,3-butadiene.

EPA Response: The references cited for the impact of genetic polymorphisms, namely Abdel-Rahman et al., 2001, 2003, and 2005, were considered in the systematic literature review for 1,3-butadiene and included in the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d). They are cited for their evidence of 1,3-butadiene mutagenicity. The 2001 paper has also been added to the PESS table for providing evidence that microsomal epoxide hydrolase mutations can lead to increased susceptibility for mutations.

1,3-Butadiene emissions to air and water were considered in the *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* (U.S. EPA, 2025p). EPA assessed exposures to populations in fenceline communities and other PESS groups as described in Sections 5.3.4, 5.3.5, and 7.1.5 of the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g). As described in the *Scope of the Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2020b), exposures resulting from accidents, spills, and other releases are outside the scope of the risk evaluation because they cannot be reliably predicted or reasonably foreseen. Additionally, EPA is not considering acute risks from 1,3-butadiene exposure, and therefore an accident or rare spill would not be relevant for chronic risks. See comment 3.7.11 for more details on spills. Although cigarette smoking results in exposure to 1,3-butadiene, it is outside the scope of the risk evaluation as described in Section 2.2 of the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g) (note that all sources of substances in the environment are included in ambient air modeling with AirToxScreen; thus, tobacco smoke was qualitatively assessed in Section 2.3.3.2 of *General Population Exposure for 1,3-Butadiene* (U.S. EPA, 2025c)).

2.5 Aggregate Exposures and Cumulative Risk

2.5.1 Comment

Summary: One public commenter on the 2018 docket (EPA-HQ-OPPT-2018-0451-0060) and several commenters on the 2024 docket (EPA-HQ-OPPT-2024-0425-0088, 0105, 0116, 0069, 0079, 0092) noted that EPA underestimated risks by not adequately considering aggregate and cumulative exposures, including those from multiple facilities, unintended releases, and background sources like vehicle exhaust and tobacco smoke. One public commenter (0092) noted that EPA's supplement does not account for aggregate exposures from multiple facilities, potentially underestimating real-world cancer risks. For example, two facilities in Orange, TX were analyzed separately, ignoring the combined exposure from multiple nearby emitters. One commenter (0079) also suggested aggregating across exposure sources such as occupational, background, and from fenceline exposure for those who may be part of multiple PESS groups.

EPA Response: The final risk evaluation aggregates exposures for estimation of both non-cancer and cancer risks (Section 5.3.4, 5.3.5, and 5.3.6). The Toxic Substances Control Act (TSCA) does not require EPA to conduct cumulative risk assessments, although the Agency may complete cumulative assessments on a chemical-specific basis when the best available science indicates that it is an appropriate course. At this time EPA is not performing a cumulative risk assessment for 1,3-butadiene. The Agency notes that a *Draft Proposed Approach for Consideration of Chemical Co-exposure in TSCA Risk Evaluations* was published and peer-reviewed in 2024 and may inform future risk evaluations (U.S. EPA, 2024b). The exposure assessment considered monitoring information including for ambient air outside of facilities that use 1,3-butadiene in conjunction with modeled exposures for the general population based on reported releases from industrial sites (*General Population Exposure Assessment for 1,3-Butadiene* Section 2.3.1). For this fit-for-purpose TSCA risk assessment, the EPA did qualitatively consider and contextualize multiple sources of 1,3-butadiene, including automobile exhaust (onroad and nonroad mobile sources), residential wood burning, natural fires through the AirToxScreen discussion in Section 2.3.2.2 of the *General Population Exposure for 1,3-Butadiene* (U.S. EPA, 2025c). Thus, measured background concentrations were considered as part of the body of evidence for general population exposures to 1,3-butadiene including as context for measured and modeled concentrations that were directly related to TSCA conditions of use.

3 Public Comments Posted on EPA-HQ-OPPT-2024-0425

1,3-Butatdiene public comments on the docket numbered EPA-HQ-OPPT-2024-0425 are summarized in the subsections below.

Table 3-1. Index of Public Comment Submissions to Docket EPA-HQ-OPPT-2024-0425, Sorted by Submission Number

Submission Number	Commenter Name
EPA-HQ-OPPT-2024-0425-0052	American Chemistry Council (ACC)
EPA-HQ-OPPT-2024-0425-0053	American Industrial Hygiene Association (AIHA)
EPA-HQ-OPPT-2024-0425-0054	Temitope Asefon
EPA-HQ-OPPT-2024-0425-0055	Grand Valley State University
EPA-HQ-OPPT-2024-0425-0058	Nuclear Energy Institute (NEI)
EPA-HQ-OPPT-2024-0425-0059	Rachel Braaten
EPA-HQ-OPPT-2024-0425-0060	National Tribal Toxics Council
EPA-HQ-OPPT-2024-0425-0067	Celanese
EPA-HQ-OPPT-2024-0425-0068	Alliance for Chemical Distribution (ACD)
EPA-HQ-OPPT-2024-0425-0069	University of CA, San Francisco Program on Reproductive Health and the Environment (UCSF PRHE)
EPA-HQ-OPPT-2024-0425-0073	Anonymous
EPA-HQ-OPPT-2024-0425-0076	American Chemistry Council (ACC)
EPA-HQ-OPPT-2024-0425-0077	Household and Commercial Products Association (HCPA)
EPA-HQ-OPPT-2024-0425-0079	Environmental Defense Fund (EDF)
EPA-HQ-OPPT-2024-0425-0080	Dow Chemical Company
EPA-HQ-OPPT-2024-0425-0081	Boeing Company
EPA-HQ-OPPT-2024-0425-0082	U.S. Tire Manufacturers Association (USTMA)
EPA-HQ-OPPT-2024-0425-0083	INV Nylon Chemicals Americas, LLC
EPA-HQ-OPPT-2024-0425-0084	American Fuel & Petrochemical Manufacturers (AFPM)
EPA-HQ-OPPT-2024-0425-0085	Alliance for Automotive Innovation (AAI)
EPA-HQ-OPPT-2024-0425-0087	American Chemistry Council (ACC)
EPA-HQ-OPPT-2024-0425-0088	Beaver County Marcellus Awareness Community et al., (1 of 4)
EPA-HQ-OPPT-2024-0425-0089	Beaver County Marcellus Awareness Community et al., (2 of 4)
EPA-HQ-OPPT-2024-0425-0090	Beaver County Marcellus Awareness Community et al., (3 of 4)
EPA-HQ-OPPT-2024-0425-0091	Beaver County Marcellus Awareness Community et al., (4 of 4)
EPA-HQ-OPPT-2024-0425-0092	University of CA, San Francisco Program on Reproductive Health and the Environment (UCSF PHRE)
EPA-HQ-OPPT-2024-0425-0100	Carlos Santos Burgoa/SACC Member

Submission Number	Commenter Name
EPA-HQ-OPPT-2024-0425-0101	Christine Chaisson/SACC Member
EPA-HQ-OPPT-2024-0425-0102	Penelope Fenner-Crisp/SACC Member
EPA-HQ-OPPT-2024-0425-0103	George Cobb/SACC Chair
EPA-HQ-OPPT-2024-0425-0104	Chris Kirman/SciPinion, LLC
EPA-HQ-OPPT-2024-0425-0105	Veena Singla/Columbia University
EPA-HQ-OPPT-2024-0425-0106	MacKinsey Bach/ExxonMobil Biomedical Sciences, Inc.
EPA-HQ-OPPT-2024-0425-0107	Craig Warren Davis/Exponent
EPA-HQ-OPPT-2024-0425-0108	Paul DeLeo/American Chemistry Council
EPA-HQ-OPPT-2024-0425-0109	Neeraja Erraguntla/American Chemistry Council
EPA-HQ-OPPT-2024-0425-0110	Sylvia Maberti/ExxonMobil Biomedical Sciences, Inc.
EPA-HQ-OPPT-2024-0425-0111	Julie Panko/ToxStrategies
EPA-HQ-OPPT-2024-0425-0112	Alan Rovira/Shell Global Solutions Inc.
EPA-HQ-OPPT-2024-0425-0113	Alan Rovira/Shell Global Solutions Inc.
EPA-HQ-OPPT-2024-0425-0114	Dan Baker/Consultant
EPA-HQ-OPPT-2024-0425-0115	Jim Cooper/American Fuel & Petrochemical Manufacturers (AFPM)
EPA-HQ-OPPT-2024-0425-0116	University of California, San Francisco Program on Reproductive Health and the Environment (UCSF PHRE)
EPA-HQ-OPPT-2024-0425-0117	George Cobb/SACC Chair
EPA-HQ-OPPT-2024-0425-0118	American Fuel & Petrochemical Manufacturers (AFPM)
EPA-HQ-OPPT-2024-0425-0119	Rainbow Rubin/SACC member
EPA-HQ-OPPT-2024-0425-0120	Wendy Heiger-Bernays/SACC member
EPA-HQ-OPPT-2024-0425-0122	Veena Singla/Columbia University
EPA-HQ-OPPT-2024-0425-0125	American Chemistry Council (ACC)

3.1 General

3.1.1 Comment

Summary: A public commenter (0054) advocated for stronger regulatory oversight, especially for industries that rely on 1,3-butadiene. The commenter stated that even though economic considerations are important, the protection of human health and the environment must remain the highest priority. The commenter urged the agency to take precautionary actions when risks are uncertain or potentially severe.

EPA Response: The EPA acknowledges the comment. TSCA requires EPA to make unreasonable risk determinations without consideration of cost or other non-risk factors. Such considerations may be considered during rulemaking under TSCA section 6(a).

3.1.2 Comment

Summary: An anonymous commenter (0073) recommended the adoption of Biden Administration policy (unspecified) on 1,3-butadiene.

EPA Response: Without further details on the specific policy recommended by the commenter, the EPA is unable to determine how to incorporate this suggestion into the risk evaluation.

3.1.3 Comment

Summary: A public commenter (0084) raised concerns about potential limitations of the considered OES, stating that manufacturing scenarios related to paint coatings, adhesives and sealants and fuels would not result in exposure to 1,3-butadiene but instead to polymers made from butadiene. Another concern of the commenter was that the process description for the OES of recycling (*i.e.* combining recycled butadiene with crude streams for energy recovery, incorporating as feedstock for ethylene production, and other described processes) may not be relevant as a meaningful exposure scenario. The reasoning stated is that processes such as ethylene production take place in closed systems at highly regulated facilities, leading to a low likelihood of exposure.

EPA Response: EPA designated 1,3-butadiene as a High-Priority Substance in December 2019 and initiated a risk evaluation on this substance (40 CFR 702, subpart A). Monitoring data from 1,3-butadiene facilities have detected the presence of 1,3-butadiene monomer in workplace air. Additionally, release data from the TRI show that the 1,3-butadiene monomer is primarily released into the environment through air emissions.

3.1.4 Comment

Summary: A public commenter (0053) agreed that 1,3-Butadiene should be a high-priority substance for risk evaluation.

EPA Response: The comment has been noted. 1,3-Butadiene was designated as a high-priority substance in December 2019 through EPA's chemical prioritization process, as defined under TSCA.

3.1.5 Comment

Summary: A public commenter (0055) suggested enhancing the risk evaluation with advanced predictive modeling techniques, time-series analysis for exposure trends, clustering methods for subpopulation sensitivity, and improved transparency in model validation to refine methodologies and analyses.

EPA Response: EPA currently uses the Human Exposure Model (HEM), which serves as a predictive modeling technique specifically tailored for environmental exposure and risk assessment. HEM provides a robust framework by integrating geographic information systems (GIS) for spatial analysis and using dispersion models like AERMOD to predict pollutant concentrations under varying meteorological conditions. This allows us to estimate potential human exposure levels and assess associated health risks effectively. We validate our models with available monitoring data to ensure their accuracy and reliability. While we acknowledge the benefits of time series analysis in identifying temporal trends, HEM's holistic approach aligns well with our current objectives. EPA will explore the integration of time series analysis where appropriate to further enhance its assessments.

In identifying PESS, EPA employs a comprehensive approach utilizing demographic analysis, geospatial analysis, health outcome data analysis, epidemiological studies, and toxicological and physiological assessments (See Section 5.3.5 of the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA,

2025g)). These methods collectively provide a robust framework for accurately identifying vulnerable groups and ensuring their protection in our assessments. While we are confident in the sufficiency of our current approach, we remain committed to continually improving our methodologies to enhance our understanding and protection of these subpopulations.

3.2 Conditions of Use

Comments associated with this issue are summarized in the subsections below.

3.2.1 Comment

Summary: One commenter (0081) requested clarification on the categorization of polyurethane potting and casting compounds, used in applications for aerospace and defense, which do not fit neatly within EPA's current COU definitions, suggesting inclusion in the Adhesives and Sealants COU or establishing a new COU. The commenter's concern was that materials used in aerospace and defense applications require an intensive process to ensure compliance with performance criteria set by the FAA and DOD. 1,3-butadiene is a component of various aircraft systems, but the commenter indicates a particularly notable role as a conformal coating to protect circuit boards to prevent electrical shorts and premature failures, with a potting compound used to encapsulate electronic parts for electrical insulation. Most of the aerospace uses fall under COUs categorized by EPA as not significantly contributing to unreasonable risk. However, the use case of potting and casting compounds providing a sealant function does not neatly fall into EPA's current COU definitions and the commenter requested either clarifying whether this falls under the Adhesives and Sealants COU or considering establishment of a new COU that would cover this use case.

EPA Response: EPA has now referenced polyurethane potting and casting compounds, with applications in the defense and aerospace sectors, into the COU description for Industrial use of Adhesives and Sealants, Including Epoxy Resins (See Appendix E of the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g)).

3.2.2 Comment

Summary: One commenter (0082) noted the need for EPA to accurately distinguish between different OESs relating to rubber tire manufacturing, as they involve different manufacturing processes and exposure conditions. Specifically, "rubber polymerization" does not occur at tire manufacturing facilities, whereas "rubber compounding" and "rubber converting" do. Similarly, another commenter (0111) pointed out that the manufacturing of synthetic rubber should be assessed as processing as a reactant, rather than as plastic and rubber compounding. Another commenter (0083) questions their facility's inclusion in the Plastics and Rubber Compounding category. They provide data supporting that 1,3-butadiene is fully consumed early in their process and suggest the EPA refine its analysis to reflect this.

EPA Response: EPA agrees that the 1,3-butadiene polymerization process was erroneously assessed in the same category as Plastics and rubber compounding. To correct this, EPA has added a new occupational exposure scenario (OES) to the risk evaluation, which quantifies releases and exposures due to the polymerization of 1,3-butadiene (as opposed to the downstream processes of rubber compounding and converting). This OES is named Plastics and rubber polymerization and can be found in Section 3.5 of the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene* (U.S. EPA, 2025p). The Plastics and rubber compounding and Plastics and rubber converting OESs have been combined into a single OES called Plastics and rubber compounding and converting and can be found in Section 3.6 of the same document.

Regarding comment 0083, EPA has determined that the Orange site referred to in the comment was erroneously mapped to the Plastics and Rubber Compounding OES in both 2017 and 2020 NEI. NEI indicates, however, that in 2017 and 2020 this facility manufactured adiponitrile which would fall under Processing as a Reactant. In the final risk evaluation, the Orange facility was recategorized to be under the Processing as a Reactant OES.

3.2.3 Comment

Summary: One commenter (0077) recommended that EPA expand the description and characterization of 1,3- butadiene as a reactant in propellant manufacturing by the United States Department of Defense (DOD). The commenter suggested that a consistent definition of "propellant manufacturing" is also recommended, as it is described as "rocket propellant," "space vehicle propellant," and simply "propellant" at other points. This would reduce the potential for confusion with aerosol propellant manufacturing and processing and corresponding occupational exposure scenarios.

EPA Response: Additional context provided by the commenter related to propellant use is now referenced in EPA's COU description for Processing – Reactant – Intermediate (Adhesive manufacturing; all other basic organic chemical manufacturing; fuel binder for solid rocket fuels; organic fiber manufacturing; petrochemical manufacturing; petroleum refineries; plastic material and resin manufacturing; propellant manufacturing; synthetic rubber manufacturing; and paint and coating manufacturing) (see Appendix D of the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g)).

3.3 Butadiene Polymers

3.3.1 Comment

Summary: A commenter (0115) noted that the evaluation conflates butadiene monomer with copolymers and incorrectly identifies butadiene as an ingredient in various products, whereas it is consumed as an intermediate.

EPA Response: Although 1,3-butadiene is largely consumed as an intermediate in the polymerization process as described in Section 3.14.1 of the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene* (U.S. EPA, 2025p), residual amounts of 1,3-butadiene were reported in several types of products including architectural paints and coatings, and resins (ACA, 2019). It is also reported as a constituent in some adhesives, resins, and propellants (EPA-HQ-OPPT-2018-0451-0009), and it was listed as a component in a tire patch product (Highline Warren, 2015). See Sections 3.9.1 and 3.10.1 of the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene* for more information about these cases (U.S. EPA, 2025p). EPA attempted to reach out to the relevant companies to verify the exact form of butadiene in the product, but unfortunately, was not successful in obtaining confirmation. Nonetheless, EPA conducted analysis with the assumption that 1,3-butadiene is present in its gaseous form in these products, and we maintain a slight confidence in the findings based on this assumption.

3.4 Environmental Exposures

3.4.1 Comment

Summary: One commenter (0053) agreed with EPA's conclusion that industrial releases to water and soil are relatively low, and that 1,3-butadiene will likely evaporate quickly into the air based on its physical and chemical properties.

EPA Response: The physical chemical properties of 1,3-butadiene suggest that 1,3-butadiene will likely evaporate quickly into the air based on a Henry's Law Constant of 0.076 atm m^3/mol at 25 °C and water solubility of 735 mg/L at 20°C as stated in Section 3.1 of the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g). Annual releases of 1,3-butadiene to water (≤ 0.1% of total 1,3-butadiene releases) and soil (1–3% of total 1,3-butadiene releases) are relatively low based on releases reported in TRI. See Section 3 of the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene* for details (U.S. EPA, 2025p).

3.4.2 Comment

Summary: One commenter (0088) noted that the EPA failed to evaluate all relevant pathways for 1,3-butadiene, including volatilization from water and soil, which could contribute to inhalation risks

EPA Response: EPA determined that volatilization of 1,3-butadiene from water or soil surfaces will not result in underestimation of exposures for the following reasons. Available release data (TRI and DMR) indicate that 1,3-butadiene is not typically released to water and soil. In addition, 1,3-butadiene exhibits very low solubility in water (735 mg/L at 25°C) and a high vapor pressure (1,900 mm Hg at 20°C) indicating that it partitions overwhelmingly to the air compartment. Therefore, omission of the volatilization process does not overlook any exposure beyond those already addressed through the inhalation exposure assessment. Additional details on releases can be found in Section 2.3 of the *Environmental Release and Occupational Exposure Assessment* (U.S. EPA, 2025p). Additional details on physical chemical properties of 1,3-butadiene can be found in Section 2 of the *Physical Chemistry, Fate, and Transport Assessment for 1,3-Butadiene* (U.S. EPA, 2025f). Measured data obtained from the WQP database confirms that 1,3-butadiene is not typically found in soil and water as 100 percent of groundwater and surface water samples were below the limit of detection. Additional details on releases and sampling data can be found in Section 4 and 5 of the *Environmental Media Concentrations for 1,3-Butadiene* (U.S. EPA, 2025b).

3.4.3 Comment

Summary: One commenter (0060) disagreed with the draft evaluation's conclusion that 1,3-butadiene poses no unreasonable risk to the environment, particularly terrestrial fauna. They note that many terrestrial organisms have limited ranges and may experience similar risks as humans.

EPA Response: EPA conducted a quantitative screen of the potential risk of 1,3-butadiene to terrestrial organisms via inhalation in ambient air using rodent toxicity data from human health hazard studies. Specifically, the highest modeled and monitored concentration of 1,3-butadiene in ambient air, described in Sections 2.2.3 and 2.31 of the *General Population Exposure for 1,3-Butadiene* (U.S. EPA, 2025c), are two orders of magnitude lower than the most sensitive toxicity endpoint from human health animal models[1] (rats, mice) and no significant effects were measured on apical endpoints (*i.e.*, growth, reproduction); thus, risk to terrestrial organisms is not expected.

[1] A human health animal model is a non-human animal used in studies designed to research human health (diseases, treatments, etc.).

3.5 Environmental Risk Characterization

3.5.1 Comment

Summary: One commenter (0107) agreed that 1,3-butadiene is a highly volatile gas with limited release to soil or surface water and is not likely to be present in water or soil. Additionally, the commenter (0107) noted that exposure of aquatic and terrestrial ecological receptors to 1,3-butadiene is expected to be extremely low and of short duration. In summary, the commenter (0107) noted that EPA's conclusion to qualitatively assess the environmental risk characterization of 1,3-butadiene is supported based on the totality of evidence. Two other commenters (0108, 0115) also supported EPA's qualitative approach to environmental risks.

EPA Response: We acknowledge the commenters' support, and the modeled QSAR toxicity predictions referenced relative to surface water concentrations. The environmental risk characterization has been strengthened with animal toxicity data from human health hazard studies and quantitative screening of potential risk to terrestrial organisms via ambient air exposure (see Section 6.3 Environmental Risk Characterization in the Risk Evaluation).

3.6 Occupational Exposures

3.6.1 Comment

Summary: One commenter (0425-0053) stated that large amounts of 1,3-butadiene may be released into the work environment air by industrial sources, primarily in the production of synthetic rubbers and polymers, and that potential worker exposures to 1,3-butadiene can primarily occur "during petroleum refining and related operations, including production of petroleum refinery distillation products (C4 fractions) contain 1,3-butadiene and production and distribution of gasoline, production of purified 1,3-butadiene monomer, production of various butadiene-based rubber and plastics polymers and other derivatives, and manufacture of rubber and plastics products such as tires, hoses and a variety of similar molded objects." This commenter (0425-0053) also stated that workers involved in the production of rubber, plastics, and resins are likely exposed to the highest levels of 1,3-butadiene and provided EPA with a list of studies that monitored occupational exposure to 1,3-butadiene.

EPA Response: The studies used in this risk evaluation are presented in the relevant OES sections in Section 3 of the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene* (U.S. EPA, 2025p). To see how the exposure results were calculated in more detail, and the extracted exposure data and calculations can be found in the Supplemental file named *1,3-Butadiene Inhalation Monitoring Data Summary* (U.S. EPA, 2025k). For a list of all the occupational exposure studies considered and their rating in systematic review, see the *Data Quality Evaluation and Data Extraction Information for Environmental Release and Occupational Exposure for 1,3-Butadiene* (U.S. EPA, 2025m).

Specific to this comment, four studies were presented, and EPA has considered each of them as summarized below.

- NIOSH 1990, a National Occupational Exposure Survey, was conducted from 1981 to 1983 and found air concentrations at six facilities ranging from 0.06 to 39 ppm. EPA could not find the reference for this study, however EPA determined that more recent data would be most appropriate for this risk evaluation. This may refer to Fajen et al. (1990), which was considered

for the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d). This likely has similar data to Fajen et al. (1993), described below.

- Fajen et al. (1993) was considered. The study contains summary statistics on a number of tasks within a facility that manufactures 1,3-butadiene. The study received a systematic review rating of high. However, this source is from 1993, which is prior to the lowering of the permissible exposure limit for 1,3-butadiene in 1997 which decreased the PEL from 1,000 ppm to 1 ppm. Due to the publication date, this source likely does not represent present day exposures as accurately as other sources obtained through systematic review and public comments. Akerstrom et al. (2016) was considered. While it received a high rating in systematic review, it was not considered in estimating exposures because the study took place in Sweden, and EPA had discrete data from facilities within the United States to characterize exposures for Processing as a Reactant (see Section 3.3.4.3 in the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene* (U.S. EPA, 2025p)). Where possible, EPA prefers to use discrete datasets from the United States in the risk evaluation. When comparing EPA's exposure results for processing as a reactant during turnaround activities, EPA's estimates were one to two orders of magnitude higher than the medians presented in this study.
- Scarselli et al. (2017) was considered in the risk evaluation and received a medium rating during systematic review. The study compiled 1,3-butadiene exposure measurements from a variety of economic sectors in Italy between the years of 1996 and 2015. EPA determined that discrete data from more specifically described sources and from the United States would be more representative of occupational exposures, particularly due to the broad nature of each of the sectors, which made it difficult to understand the context behind each of the results. When comparing the study's median for "Manufacture of chemicals and chemical products", it was within the same order of magnitude as exposure for 1,3-butadiene's manufacturing OES. Similarly, the study's exposure results for "Manufacture of rubber and plastic products" and "Plastic-products machine operators", with medians of 0.11 ppm and 0.23 ppm respectively, were consistent with EPA's finding for plastics and rubber polymerization which had a 50th percentile of 0.40 ppm.

3.6.2 Comment

Summary: One commenter (0080) recommended that EPA apply the principles outlined in the 1,3-Butadiene Draft Risk Evaluation for consumers (*i.e.,* determined exposure to residual monomer in downstream articles to be very low and not require an exposure assessment) to all other COUs where 1,3-butadiene has already been incorporated into a polymer. The commenter (0080) stated that EPA could exclude Processing – Incorporation into an article, Processing – Recycling, Industrial use – Adhesives and sealants, all COUs in the commercial life cycle stage, and Disposal from the Risk Evaluation or evaluate them qualitatively. Similarly, one commenter (0084) identified errors in the EPA's OESs, such as including butadiene in products where it is not present (*e.g.*, adhesives, paints, and plastics), and calls for the removal of these scenarios from the risk evaluation. Another commenter (0115) noted that the evaluation conflates butadiene monomer with copolymers and incorrectly identifies butadiene as an ingredient in various products, whereas it is consumed as an intermediate.

EPA Response: Although 1,3-butadiene is largely consumed as an intermediate in the polymerization process as described in Section 3.14.1 of the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene* (U.S. EPA, 2025p), residual amounts of 1,3-butadiene were reported in several types of products including architectural paints and coatings, and resins (ACA, 2019). It is also reported as a constituent in some adhesives, resins, and propellants (EPA-HQ-OPPT-2018-0451-0009), and it was listed as a component in a tire patch product (Highline Warren, 2015). See Sections 3.9.1 and

3.10.1 of the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene* for more information about these cases (U.S. EPA, 2025p).

3.6.3 Comment

Summary: Several commenters (0082, 0087, 0109) challenged the EPA's assumption that ONUs have exposure levels equal to workers, suggesting instead that ONU exposure should be lower. One commenter (0111) also noted that the evaluation of ONU exposures should be consistent with the EPA's definition, which indicates that ONUs do not have direct exposure; therefore, their exposure should be assumed to be lower than that of workers. Additionally, OSHA standards mandate restricted areas for ONUs, and utilizing ACC's submitted data could assist in establishing an ONU factor or ratio for scenarios where direct data are unavailable.

EPA Response: If available, it is EPA's preference to estimate central tendency and high-end ONU exposures from applicable ONU data. However, in the absence of such a dataset, EPA typically uses the central tendency of worker exposures to approximate ONU exposures. This is the method that was used to assess ONU exposure for six OESs including Repackaging, Plastic and rubber compounding and converting, Application of paints and coatings, Application of adhesives and sealants, Recycling, and Waste handling, treatment, and disposal. As stated by the commenters, workers are typically expected to experience higher exposures overall than ONUs because workers are handling the chemical while ONUs are in the same area with the chemical but not handling it. However, the high-end concentrations an ONU may experience can be above the central tendency worker concentration. An example of this can be seen in the inhalation exposure data used to assess the 8-hour Manufacturing OES in Table 5-1 in the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene* (U.S. EPA, 2025p). These estimates were calculated using inhalation monitoring data from *Analysis of 1,3-Butadiene Industrial Hygiene Data* (ToxStrategies, 2021). The high-end exposure for the ONU similar exposure group (SEG) is higher than 11 out of the 15 central tendency exposures for worker SEGs. To reduce the possibility of underestimating ONU exposure, EPA chose to maintain the current method of estimating ONU exposure using the central tendency worker exposure in the absence of more applicable monitoring data.

3.6.4 Comment

Summary: Several commenters (0083, 0110, 0115) stated that EPA's use of detection levels for non-detect readings in exposure assessments was overly conservative and not reflective of most collected data.

EPA Response: The substitution of the detection limit for measurements below the limit of detection is only used in one instance, to estimate the conservative high-end occupational exposure for the Application of Adhesives, Sealants, Paints and Coatings OES. Because MOEs for the high-end exposures for this OES were not below the benchmark, there was not a need to further refine the substitution approach.

In other cases where a large portion of a dataset was non-detect (or censored), for the final risk evaluation EPA conducted additional analysis of the datasets. EPA determined that maximum likelihood estimation (MLE) assuming a lognormal distribution of concentrations was the best method to produce 50th and 95th percentiles (to represent central tendency and high-end respectively) for highly censored datasets that had five or more uncensored datapoints. Section 2.4.3.1 of the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene* describes EPA's modified method for incorporating measurements below the limit of detection (U.S. EPA, 2025p). More information about EPA's use of MLE, and a summary of the options for highly censored data considered for this risk

evaluation, can be found in Appendix H of the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene* (U.S. EPA, 2025p). In cases where there were too few measured datapoints (less than five) to perform a more robust analysis such as MLE, EPA estimated the exposure concentrations for these data following EPA's Guidelines for Statistical Analysis of Occupational Exposure Data (EPA, 1994) which recommends using the LOD/√2 if the geometric standard deviation of the data is less than 3.0 and LOD/2 if the geometric standard deviation is 3.0 or greater.

3.6.5 Comment

Summary: Several commenters (0084, 0115, 0111) disagreed with EPA's use of task-based exposures to represent 8-hour shift exposures, stating them as unrealistic and leading to overestimated exposure levels. One commenter (0111) noted that for repackaging, recycling, and waste handling scenarios, short-term task-length data from the submitted report *Analysis of 1,3-Butadiene Industrial Hygiene Data* (ToxStrategies, 2021) was incorrectly utilized as 8-hour and 12-hour TWA estimates, and stated that the activities performed during the task-length samples differ from the worker activities EPA described in the relevant OESs' worker activity sections. Another commenter (0084) also stated that the use of manufacturing data as analog for repackaging is not appropriate because those use scenarios involve transfers between containers during transportation and assume accidental releases during each transfer.

EPA Response: In the draft assessment, EPA used task-length exposure monitoring to estimate full-shift exposures for the OESs of Repackaging, Recycling, and Waste handling, treatment, and disposal. This "full-shift assumption" assumed that the measured task-length exposure occurs through the entirety of a shift. In the final risk evaluation, EPA presents this "full-shift assumption" as an upper end of the possible exposure range. A "task-length assumption" was also included in the final risk evaluation to capture the lower end of the possible exposure range. This task-length assumption is the assumption that the measured exposure occurs only for the stated duration of the task with no exposure for the remainder of the 8-hour shift. EPA uses these two estimates in the final risk evaluation to "bracket" possible exposures. This method is expected to capture the range of exposures.

Regarding the use of analogous data, the OESs that utilize analogous data (Repackaging, Incorporation into formulation, Laboratory use, Recycling, and Waste handling, treatment, and disposal) have been more thoroughly discussed in the final assessment to better explain the datasets' relevance to the OESs. These descriptions are in the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene*, Sections 3.2.4, 3.4.4, 3.8.4, 3.12.4, and 3.13.4 (U.S. EPA, 2025p). Analogous data, by its definition, is not directly applicable to the scenario that it is estimating exposure for. However, given EPA's understanding of these scenarios, the activities from these task-length samples are expected to be similar to the activities that would occur during the relevant OES. For example, using the case of repackaging pointed out by commenter 0084, EPA used workers who load and unload 1,3-butadiene at a manufacturing site to estimate exposures to those workers who load and unload at a repackaging facility. Some uncertainty is inherent in this assumption, since EPA expects manufacturing facilities to load and unload from large transports such as barges, trucks, and rail car, while a repackaging facility may be using containers of various sizes including those that are smaller. A repackaging facility may also be handling 1,3-butadiene in its gaseous state while at manufacturing sites it is typically handled as a pressurized liquid. However, there are exposure potentials that are common among all transferring activities regardless of the size (connecting and disconnecting hoses and lines, cleaning transport containers, releases from the connections during the transfer itself), and so in the absence of more applicable data EPA determined that it was reasonable to use exposure data from workers who load and unload at a manufacturing site as an analog for those who load and unload at a repackaging facility. The applicability and limitations of these cases are now more thoroughly discussed in the Weight of Scientific Evidence Conclusions, Section 6.2 of the *Environmental Release and Occupational Exposure*

Assessment of 1,3-Butadiene (U.S. EPA, 2025p). EPA considered the use of models or surrogate data (data from the same OES but for a different chemical) for these OESs, however EPA did not find models that were suitable for 1,3-butadiene, nor surrogates that matched the physical properties or uses of 1,3-butadiene in the relevant settings. More applicable monitoring data were also not found for these cases.

3.6.6 Comment

Summary: One commenter (0084) stated the risk evaluation relied on incorrect assumptions about the nature of the laboratory use, such as EPA's assumption that unconsumed 1,3-butadiene will be "disposed of with other laboratory wastes", which the commenter stated is unrealistic in any type of industrial or academic laboratory setting. The commenter also pointed out that use of fume hoods and hoses create a closed system in labs when 1,3-butadiene is used in the laboratory setting, and EPA should consult with laboratories about their practices instead of speculating. Another commenter (0111) noted that the use of the data from the *Analysis of 1,3-Butadiene Industrial Hygiene Data* (ToxStrategies, 2021) as analogous for commercial use of laboratory chemicals is inappropriate due to differences in physical state, concentration purity, and the quantity of the chemical handled in manufacturing facility's laboratory versus a commercial laboratory setting.

EPA Response: Although the analyses performed in a laboratory at a manufacturing or processing site may be different than analyses performed in a commercial laboratory setting, it is reasonable to assume that in both cases the worker may be handling highly concentrated 1,3-butadiene under a hood using comparable handling methods. EPA is aware that 1,3-butadiene can be highly concentrated in a manufacturing or processing setting, and EPA is also aware of cylinders of purified 1,3-butadiene in the form of a liquified gas that are sold for use in a laboratory setting (Sigma-Aldrich, 2024). EPA considered the use of models or surrogate data (data from the same OES but for a different chemical) for this OES, however EPA did not find models that were suitable for 1,3-butadiene, nor surrogates that matched the physical properties or uses of 1,3-butadiene in the relevant settings. More applicable monitoring data were also not found for this case. It was therefore decided that the data from the laboratory technicians at manufacturing and processing facilities were the best available option for assessing this OES.

However, EPA acknowledges the commenters' concerns that using the exposure information from laboratory technicians at a manufacturing or processing site will overestimate exposures compared to a worker in a commercial laboratory setting. This is due to the factors pointed out by the commenter, and due to the different worker activities, that may occur in a manufacturing setting yet would not occur at a commercial laboratory, such as sampling of 1,3-butadiene from the process. Therefore, in the final risk evaluation, EPA assumed that the central tendency exposure values for the laboratory technician dataset are more representative for a commercial laboratory scenario than the high-end.

EPA has added additional discussion on this OES in the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene*, see Sections 3.8 (U.S. EPA, 2025p). The applicability and limitations of this case is more thoroughly discussed in the Weight of Scientific Evidence Conclusions, Section 6.2 of the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene* (U.S. EPA, 2025p).

3.6.7 Comment

Summary: One commenter (0109) recommended EPA base scenarios on realistic industry practices and use representative data for worker tenure in chemical manufacturing. Similarly, one public commenter (0111) recommended updating the occupational tenure values to better reflect present-day occupational

trends. They note that the occupational tenure value of 36 years is outdated and does not align with current industry standards. According to the Exposure Factors Handbook, the median tenure is significantly lower; 7.9 years for men, and 5.4 years for women, and for the SBR cohort from which the cancer slope factor was derived, the median tenure was 8 years.

EPA Response: EPA's explanation for occupational tenure can be found in Appendix B.2.6 of the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene* (U.S. EPA, 2025p). As described, EPA used employee tenure information from the Bureau of Labor Statistics (BLS) Current Population Survey (CPS) from 2014 and the U.S. Census Survey of Income and Program Participation (SIPP). Relevant to the SIPP data, although the tenure may differ for any given industry sector, there was no significant variability between the 50th and 95th percentile values of average tenure across manufacturing and non-manufacturing sectors.

These datasets were used to develop a triangular distribution for working years. A triangular distribution needs a minimum value, mode value, and maximum value. The minimum value, meant to represent a low-end estimate on the number of lifetime working years, was obtained from the BLS CPS median tenure data with a current employer for ages 55 to 64 years old (10.4 years). The mode value, meant to represent a middle value of the distribution, was obtained from U.S. Census SIPP data where the 50th percentile tenure data with all employers for age groups 50 plus was calculated (36 years). The maximum value, meant to represent a high-end estimate of the number of lifetime working years, was obtained from U.S. Census SIPP data where the 95th percentile tenure data with all employers for age groups 50 plus was calculated (44 years).

From this triangular distribution, a tenure of 31 years and 40 years was established for the 50th and 95th percentiles respectively. These are the values used in the risk assessment.

The values from the Exposure Factors Handbook that the commenter cites are from 1988, which is older than the data from BLS, not specific to the chemical industry, and the estimate is skewed lower than appropriate due to the inclusion of younger individuals whose tenure would not accurately reflect an individual's total working years over a lifetime.

3.6.8 Comment

Summary: One public commenter (0110) noted that EPA's calculated intermediate average daily exposures in manufacturing and processing activities are unlikely to reflect actual workplace exposure due to the short duration of frequent tasks that may cause exposure and the infrequency of infrequent tasks. Therefore, they stated that assuming a worker experiences the 95th percentile time-weighted average exposure for 22 out of 30 days would be unreasonable. The commenter also recommended that EPA consider how exposures spanning over 22 days should be effectively managed within occupational health frameworks to ensure worker safety, noting that risk evaluation results should guide risk management strategies especially within traditional occupational health programs that focus on controlling exposures at the task level.

EPA Response: EPA's exposure estimates are primarily based on full-shift estimates and not specific tasks, inclusive of both routine and less-common activities. By definition, all workers experience an intermediate exposure duration over the course of a month; intermediate is a shorter duration of repeated exposures (totaling less than 10% of a lifetime) that has been quantified based on the relevance to certain health effects. A worker's exposure may be higher over a given month compared to their yearly average based on variations in work schedule and job assignments, and EPA is applying the best available science by capturing the full range of relevant exposure durations between acute, intermediate,

and chronic scenarios. The 95th percentile values in this assessment for a given exposure group of 1,3-butadiene manufacturing and processing represent actual measured exposures based on specific tasks that a worker or group of workers is performing. While it may be unlikely that those same high-intensity exposures would be repeated every day over a 40-year career, EPA assumes that it is plausible that especially for non-routine activities or tasks, they could be repeatedly performed over the course of a month.

3.6.9 Comment

Summary: Public commenter (0076) submitted two revisions (0425-0052 followed by 0425-0076) of the *Analysis of 1,3-Butadiene Industrial Hygiene Data* report initially submitted to the EPA in public comment EPA-HQ-OPPT-2018-0451-0053. In the first revision (0052), the commenter updated the report with additional industrial hygiene metadata such as additional information about the tasks that were monitored. In the second revision (0076), the commenter identified a misclassification within the report they had previously submitted, specifically in the data point for the Laboratory Technician—nonroutine job group. The data point was originally categorized as a full-shift exposure result but actually represented a short-term exposure (less than or equal to 15 minutes) of the task called "sample collection and analysis." The revised version of the report was provided to reflect this correction.

EPA Response: EPA has updated Section 3.1.4.1 and 3.2.4.1, which focus on the worker activities for manufacturing and processing of 1,3-butadiene respectively, with the additional information provided by the commenter.

EPA acknowledges the comment that the datapoint within the Laboratory Technician – Non-routine category has been corrected, as the point is instead a short-term task-based exposure point with a duration of 15 minutes or less for the task of "sample collection and analysis". Upon the removal of this single point for the Laboratory Technician – Nonroutine from the *Analysis of 1,3-Butadiene Industrial Hygiene Data*, there is no full-shift data on the exposure to the non-routine Laboratory Technician job group, and there are no other indicia of non-routine Laboratory Technician job groups. EPA has removed this SEG (Laboratory technician – non-routine) from the risk evaluation; the other SEG groups assessed are appropriate for Laboratory Technicians.

3.6.10 Comment

Summary: One commenter (0077) encouraged EPA to expand the description and characterization of 1,3-butadiene as a reactant in propellant manufacturing by the United States Department of Defense (DOD), and establish a consistent definition of "propellant manufacturing", because there is potential for confusion between the various types of propellants mentioned in the risk evaluation which include "rocket propellant," "space vehicle propellant," and simply "propellant". The commenter also pointed out that, although aerosol propellants are known to contain residual amounts of 1,3-butadiene, they are filled in a separate "gas house" where workers are not present, and so there is no need to routinely monitoring workers at the step where aerosol propellants are filled.

EPA Response: As the commenter pointed out, in the draft risk evaluation EPA did not always specify what kind of "propellant" was being referred to. A more thorough description about the rocket propellant was not found, however in the final risk evaluation the characterization of "propellants" has been clarified by the addition of either "rocket" or "aerosol" in every case to avoid confusion between these two cases. Aerosol propellant manufacturing falls under the OES of Incorporation into formulation, mixture, or reaction product. Rocket propellant manufacturing falls under the OES of Processing as a reactant.

EPA has also incorporated the commenter's additional information about worker exposures during the process of filling aerosol propellants into Section 3.4.4.1 of the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene* (U.S. EPA, 2025p).

3.6.11 Comment

Summary: One public commenter (0077) commented on data from the Substances in Preparations in Nordic Countries (SPIN) database identifying 1,3-butadiene in aerosol propellants that was referenced in Section 3.4.1 of the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene* (U.S. EPA, 2025p). The commenter pointed out that there were no reports since 2017 that 1,3-butadiene was present in aerosol propellants, and even those reports from 2017 and earlier indicated that the use volume was 0.0 tons, and requested this context be included in the risk evaluation.

EPA Response: EPA has updated the relevant years indicating the presence of 1,3-butadiene in aerosol products from SPIN in Section 3.4.1 of the *Environmental Release and Occupational Exposure Assessment of 1,3-Butadiene* (U.S. EPA, 2025p) (the risk evaluation once indicated reports up to the year of 2016, and this was corrected to 2017). EPA also added additional context about the results from the SPIN database to describe that the volume reported in the relevant years was indicated to be 0.0 tonnes in all cases (which indicates a use volume of less than 100 kg).

3.6.12 Comment

Summary: One commenter (0082), who had submitted industrial hygiene data to EPA, recommended that EPA reconsider using the 95th percentile of their submitted dataset to assess risk due to the fact that the dataset is severely censored (75 to 100% of the data are non-detects). The commenter stated that the substitution method used to address the non-detect samples in their dataset (where one half the LOD was used in place of non-detect samples) skewed the assessment results high by excluding true "zero" concentrations, and they argued that using the mean concentration would provide a more accurate estimate of long-term exposure.

EPA Response: EPA acknowledges that the substitution method used in the draft risk evaluation may skew the 50th and 95th percentile high and has updated the method of handling high censored datasets in the final risk evaluation. In the final risk evaluation, EPA used maximum likelihood estimation (MLE) assuming a lognormal distribution of concentrations to produce 50th and 95th percentiles to represent central tendency and high-end respectively. EPA agrees with the commenter that a central concentration such as the mean or midpoint (midpoint being another term for the 50th percentile) is more representative of long-term exposure than a high-end concentration. This is reflected in the risk determination, where central tendency exposure estimates were used to represent chronic exposure scenarios.

3.6.13 Comment

Summary: One commenter (0083) requested that the EPA reconsider the data used for occupational exposure in repackaging scenarios, as a separate data source referenced within their comment indicated much lower exposure levels, and thus the commenter questioned whether the occupational exposure data used in this category are appropriate for all repackaging scenarios included under this heading. This commenter previously provided industrial hygiene data to EPA (EPA-HQ-OPPT-2018-0451-0068), though none associated with loading or unloading of 1,3-butadiene as this monitoring was managed by their contractor in charge of the loading and unloading activities. The commenter did state that the monitoring data from the contractor were non-detect and, thus, are significantly lower than the 15 ppm (high end) and 1.1 ppm (central tendency) worker inhalation estimates used by the EPA for the analysis in the draft risk evaluation. The commenter (0083) requested that EPA reconsider the applicability of the

data it used for all activities relating to receipt and storage of 1,3-butadiene and offered to meet to assist in further refining EPA's assessment.

EPA Response: It is EPA's understanding that the industrial hygiene data referred to is the following statement, located on page 7 out of 18 of the second attachment of comment EPA-HQ-OPPT-2018-0451-0068: "Occupational exposure data collected on the workers (3rd party) unloading 1,3-butadiene barges between 2004–2023 indicate breathing zone concentrations for the workers have been non-detect". EPA is unable to incorporate the provided exposure information on unloading into the risk evaluation due to the lack of metadata associated with this statement of their contractor's conclusions, such as number of samples and other more specific information about the sampling events.

3.7 General Population Exposure

3.7.1 Comment

Summary: Several commenters (0053, 0060, 0087, 0088, 0104, 0105) noted the evaluation fails to consider exposures from non-industrial sources of 1,3-butadiene, such as open and ground-level burning of municipal solid waste, cigarette smoke, wood burning, vehicle emissions, and wildfires, or as by-product of an operation. Another commenter (0113) noted that the EPA did not consider all relevant chemical release data in its fenceline exposure assessment.

EPA Response: EPA focused its environmental release assessment on total facility emissions which can include emission from both uses of 1,3-butadiene and combustion sources at the same facility or, potentially, only combustion sources from that facility. EPA also qualitatively considered and contextualized multiple sources of 1,3-butadiene, including automobile exhaust (onroad and nonroad mobile sources), residential wood burning, natural fires through the AirToxScreen discussion in Section 2.3.2.2 of the *General Population Exposure for 1,3-Butadiene* (U.S. EPA, 2025c).

3.7.2 Comment

Summary: One commenter (0080) strongly supported the refined analysis of the general population cancer risk estimates using air release input data from the National Emissions Inventory (NEI). They state that the analysis confirms that EPA should not duplicate the efforts of other Federal and State offices and programs. The commenter states that the current analysis in the 1,3-Butadiene Draft Risk Evaluation does not constitute a true tiered approach because both IIOAC and HEM rely upon the American Meteorological Society/Environmental Protection Agency Regulatory Model (AERMOD) as the base dispersion model utilizing the same limited conservative assumptions for inputs. This commenter (0080) critiqued the screening methodology in the *Draft TSCA Screening Level Approach for Assessing Ambient Air and Water Exposures to Fenceline Communities Version 1.0*. stating that the methodology is overly conservative. The commenter (0080) stated that numerous commenters including the SACC concluded that the screening level methodology "could only be used as part of a tiered approach to evaluate risk to fenceline communities and should not be used to evaluate risks in isolation." This commenter (0080) went on to urge the SACC to recommend that OPPT not conduct a fenceline air exposure assessment as EPA Office of Air and Quality Planning and Standards already regulates, and air emissions from 1,3-butadiene are regulated by the Ethylene MACT rule at their sites. The commenter (0080) highly encouraged OPPT to work with the EPA Office of Air and Quality Planning and

Standards since EPA acknowledges that the plastics and rubber sectors are highly regulated by other Federal and State agencies.

EPA Response: EPA acknowledges the commenter's support for conducting the refined analysis but disagrees with the commenter's suggestion that OPPT should just do a refined analysis with NEI. EPA implemented SACC's recommendation to use the screening analysis as part of a tiered approach to evaluate risk to fenceline communities in the 1,3-butadiene risk evaluation and does not use the screening assessment in isolation. EPA further clarified the tiered approach in Section 2.2.1 of the *General Population Exposure for 1,3-Butadiene* (U.S. EPA, 2025c) and Section 5.3.4 of final *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g). TSCA requires EPA to conduct chemical-specific risk assessments of prioritized chemicals and following the 2024 Risk Evaluation Framework Rule (89 FR 37028, May 3, 2024), OPPT conducts appropriate air exposure assessments, including for 1,3-butadiene or other HAPS that may be regulated by other programs, as part of the TSCA risk evaluation of the chemical substance under its conditions of use. OPPT has, and continues to, coordinate with EPA's Office of Air and Radiation (OAR), reviewing residual risk reviews for Clean Air Act section 112 rules and monitoring data obtained under the Clean Air Act. For the risk evaluation of 1,3-butadiene, OPPT describes some of the coordination with OAR in the revised 1,3-butadiene general population TSD and RE. This coordination included using the same models, NEI release dataset, comparing OPPT findings for 1,3-butadiene to OARs findings in the SOCMI (HON) Risk and Technology Review (RtR) as well as integrating a discussion on fenceline monitoring obtained through OAR's Clean Air Act section 114 authorities as part of the SOCMI (HON) RtR at 9 facilities which includes monitoring for 1,3-butadiene.

3.7.3 Comment

Summary: One commenter (0080), which is not a manufacturer of 1,3-butadiene but produces a crude C4 side stream that is sold for further refinement into 1,3-butadiene down the value chain, shared 1,3-butadiene fenceline air emission sample results collected under the Clean Air Act section 114. These sample results were compared to the EPA screening level modeling results for three facilities (published in the 1,3-Butadiene Draft Risk Evaluation (U.S. EPA, 2024g)). The commenter (0080) noted that EPA's modeled concentrations for fugitive emissions range between 20 to 120 times higher than their results and that, according to EPA modeled results, each facility indicates a risk above 1×10^{-6}; whereas their monitored sites only show risk in 2 samples out of 267.

EPA Response: In response to this comment, EPA has evaluated the fenceline monitoring report (https://www.regulations.gov/document/EPA-HQ-OAR-2022-0730-0091), and has included a discussion of this report in Section 2.3.2 of the *General Population Exposure for 1,3-Butadiene* (U.S. EPA, 2025c). In addition, this commenter (0080) referenced this report in support of their recommendation of using NEI release data as inputs for EPA's modeling, which EPA added in Section 5.3.4.3 of the *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g).

3.7.4 Comment

Summary: A commenter (0060) recommended that EPA consider the inhalation pathway for the open and ground-level burning of municipal solid waste, which they stated occurs regularly in Tribal and Alaska Native communities as well as rural communities. In rural Alaska, open burning without emission controls is permitted under the Class III category of the State's regulatory code 18 AAC 60, which excepts these landfills from environmental protections that would otherwise be required since 1994 under the Resource Conservation and Recovery Act (RCRA). The commenter (006) stated that "these rural municipal solid waste streams and backyard household waste streams often contain plastics, e-waste, tires, and other synthetic materials that would likely emit 1,3-butadine (along with other toxins) when burned." The commenter (0060) noted that not only would this pathway expose landfill workers to

1,3-butadiene during full day work shifts every day, residents, including children, are often within range of the smoke in these small, rural communities. The commenter (0060) provided the example of Selawik, an Inupiat Eskimo community of 809 residents, 41.7% of whom live below the poverty level, noting that the community's only school is just 4,000 ft from their solid waste disposal site.

EPA Response: EPA acknowledges that open waste burning does exist and provides context for combustion sources from burning, *e.g.,* wildfires, from the OAR AirToxScreen assessment. However, similar to wildfires, combustion activities related to open burning practices in rural and tribal communities were not included within the scope of the risk evaluation for 1,3-butadiene. In addition, EPA does not find it practicable or have the means to quantify open burning of municipal wastes due to lack of data for this specific emissions scenario.

3.7.5 Comment

Summary: Several public commenters (0087, 0105, 0109, 0114, 0125) supported using NEI data in addition to TRI data for more accurate exposure assessments. One commenter (0114) argued that TRI data lacks detail for refined modeling while NEI data offers improved inputs, especially for emissions from flaring operations.

EPA Response: In response to SACC and public comments, EPA has included Human Exposure Model (HEM) modeling of the NEI 2017 and 2020 release data in Section 5.3.4.3 of the final *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g).

3.7.6 Comment

Summary: One public commenter (0092) noted that the NEI data showed lower cancer risks compared to TRI data without explanation. Discrepancies were noted, such as a 300-fold difference in emissions estimates for the same facility. The commenters suggested using the higher risk estimates unless a strong explanation is provided.

EPA Response: EPA expanded the discussion around the HEM modeling using the NEI 2017 and 2020 release data in the revised risk evaluation and general population TSD. The detailed discussions include narrative around possible reasons for discrepancies for facilities that report to both TRI and NEI in Section 5.3.4.4 of final *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g).

3.7.7 Comment

Summary: One public commenter (0092) noted the general population exposure modeling supplement's analysis is too limited, covering only 9 facilities out of over 700 with NEI data and fails to model risks at the fenceline.

EPA Response: EPA has included HEM modeling using a larger subset of NEI 2017 and 2020 release data in in Section 5.3.4.3 of the final *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g). In addition, EPA included an evaluation of risk estimates for fenceline populations within 5 km from NEI facilities in Section 5.3.5 of the final *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g).

3.7.8 Comment

Summary: One public commenter (0088) criticized the EPA for failing to evaluate all relevant exposure routes for 1,3-butadiene including oral and dermal exposure.

EPA Response: Current monitoring data indicates that 1,3-butadiene is not present in drinking water. Its physical properties show that it exists as a gas under normal conditions and only transitions to a

liquid at temperatures that could result in frostbite if handled without proper personal protective equipment. Furthermore, our analysis of consumer products reveals that items such as plastic and rubber do not contain 1,3-butadiene in its monomer form, thereby minimizing the risk of consumer exposure.

3.7.9 Comment

Summary: Two public commenters (0112, 0113, 0114) emphasized the availability of real-time monitoring data and encouraged their use to validate and enhance the accuracy of the EPA's risk assessment models for 1,3-butadiene. One commenter (0113) concluded that ambient air monitoring is a better indicator of fugitive emissions and emergency releases than modeling due to factors like non-dilution effects and cumulative emissions. Another commenter (0114) noted the importance of consistent temporal scales between monitoring and modeled data.

EPA Response: EPA included additional details on AMTIC monitoring data with further discussion on 24-hour and 1-hour sample data and data from other monitoring networks in Section 3.1.2 of the *Environmental Media Concentrations for 1,3-Butadiene* (U.S. EPA, 2025b) and compares modeled and monitored concentrations in Section 2.3.1.1 of the *General Population Exposure for 1,3-Butadiene* (U.S. EPA, 2025c). EPA acknowledges the importance of consistent temporal scales between monitoring and modeling data, which is why monitoring data from 2016 to 2022 were evaluated to align with the TRI 2016 to 2021 release data as well as the NEI 2017 and 2020 release data. EPA also includes additional comparisons between modeled concentrations and measured concentrations to ground truth EPA's modeling results and includes discussion on additional literature provided by SACC and public commenters on measured (monitored) concentrations of 1,3-butadiene. All the comparisons and studies demonstrated EPA's modeling approach generally does not overestimate ambient concentrations of 1,3-butadiene relative to those measured concentrations and strengthens EPA's use of modeled results to derive risk estimates and inform risk determinations.

3.7.10 Comment

Summary: One commenter (0079) noted flaws in EPA's NEI analysis. They stated that the draft HEM NEI analysis inappropriately excluded releases from certain facilities based on differences in NAICS codes and that EPA seems to have switched columns G and H, or "stack height ft" and "exit gas temperature f." resulting in an underestimation of risk.

EPA Response: EPA has investigated the example of excluded data pointed out by the commentor using NEI data from 2017 and 2020 and cannot find an instance relevant to this site (Shell Chemical LP – Norco Chemical Plant East Site) where any 1,3-butadiene point source release data was excluded. The primary NAICS code of this facility is 324110. EPA cannot find an instance where the NAICS code of this facility is 325199.

EPA included all reported release data from TRI and NEI point sources in the risk evaluation, regardless of the sources' NAICS code. The only exceptions are instances in NEI where the release of 1,3-butadiene appeared to result from 1,3-butadiene formed as a byproduct of combustion (*e.g.*, exhaust emissions). EPA posits it is more appropriate to evaluate the potential risks arising from this combustion byproduct within the scope of the risk evaluation for fuel from which the 1,3-butadiene is produced, rather than the 1,3-butadiene risk evaluation.

In addition, EPA has investigated the issue with columns G and H, or "stack height ft" and "exit gas temperature f.", and discovered that the columns were switched, specifically for the NEI 2020 dataset. This was corrected by switching the data values to correct header, applying the appropriate unit conversions and remodeled accordingly with HEM.

3.7.11 Comment

Summary: One commenter (0079) stated that EPA should consider foreseeable accidental releases and should use monitoring data to include these exposures. They additionally stated that EPA should consider background exposures and should also quantify exposures from Distribution in Commerce (which may include accidental releases from transportation). Another commenter (0069) highlighted an explosion and fire at a Texas facility and winter storm events as examples that should be included in release estimates.

EPA Response: EPA generally does not include in the scope of the risk evaluation catastrophic accidents, extreme weather events, and other natural disasters if such events do not lead to regular and predictable exposures associated with a given condition of use. Although storms, accidents, and other background exposures were not evaluated as TSCA COUs, releases from those events were included in the information that informed the 1,3-butadiene risk evaluation, including the TRI database and ambient air monitoring information. EPA used TRI-reported air emission data to estimate ambient air concentrations from TSCA COUs, using the Integrated Indoor/Outdoor Air Calculator (IIOAC) and Human Exposure Model (HEM). TRI emission data include releases from start up, shutdown, and malfunction events, since the TRI release definition broadly covers any spilling, leaking, pumping, pouring, emitting, emptying, discharging, injecting, escaping, leaching, dumping, or disposing into the environment of any toxic chemical (40 CFR 372.3). Specifically, in Part II, Section 8.8, an owner/operator must report the quantity of any release of a toxic chemical into the environment or transferred off-site as a result of a remedial action, catastrophic event, or one-time event not associated with production processes.

1,3-Butadiene is a gas at atmospheric pressure and is only liquid under high pressures. In the event of a spill, 1,3-butadiene would volatilize rapidly. While this may present an acute exposure to the general population, our assessment did not establish an acute hazard POD associated with 1,3-butadiene. Further, monitoring data have shown no measured concentrations of 1,3-Butadiene in surface or groundwater. See response to comment 1.1.1.11.

See Section 3.7 of the *Environmental Release and Occupational Exposure Assessment for 1,3-Butadiene* for full text on spills, leaks, and accidents (U.S. EPA, 2025p).

3.8 Consumer exposure

3.8.1 Comment

Summary: One commenter (0080) agreed with EPA's qualitative consumer assessment related to articles derived from butadiene-based polymers such as (but not limited to) acrylonitrile-butadiene-styrene resins and styrene-butadiene rubber. While another commenter (0053) stated that although 1,3-butadiene has been measured at very low levels in plastic or rubber of food containers, it has not been found often in food samples.

EPA Response: EPA has identified consumer COUs for 1,3-butadiene, all associated with the use of plastic and rubber products, including synthetic rubbers. Based on product searches and data identified from systematic review, EPA has determined that 1,3-butadiene, a monomer used in polymer-derived consumer products such as synthetic rubbers, is stable in these consumer products and not expected to degrade and expose the consumer to the 1,3-butadiene monomer. Residual butadiene concentrations in polymers and downstream concentrations are very low and often not detectable. EPA's final *Risk*

Evaluation for 1,3-Butadiene (U.S. EPA, 2025g) also includes a sensitivity analysis for consumer exposure and risk estimates using the Consumer Exposure Model (CEM) in Section 5.3.3.

3.9 Human Health Hazard Assessment (Non-Cancer/Overall)

3.9.1 Comment

Summary: Two public commenters (0088, 0116, 0069) disagreed with EPA for not using ovarian atrophy as the most sensitive endpoint for deriving the point of departure in its risk assessment, arguing that use of a different endpoint could underestimate the chemical's hazards. It was also suggested that EPA did not consider financial conflict of interest in the Kirman 2012 study from which the proposed mode of action was based.

EPA Response: EPA under TSCA must assess chemical risk based on the best available science. Based on the most updated understanding of 1,3-butadiene toxicokinetics and mechanistic information, the point of departure (POD) for ovarian toxicity observed in mice is not applicable to humans as humans are likely orders of magnitude less sensitive (see Section 4.1.1 of the Human health Hazard Assessment). The SACC peer reviewers concurred with EPA's determination that the ovarian toxicity POD should not be used for human health risk assessment. As for conflict of interest, EPA performs a robust systematic review of all data considered for the risk evaluation using consistent data evaluation criteria. EPA carefully evaluates all assumptions and interpretations from submitted studies and does not rely on the interpretations of study authors. However, all data are given equal consideration and EPA does not apply a more or less rigorous process to one data source versus another.

3.9.2 Comment

Summary: Three public commenters (0109, 0104, 0125) suggested that EPA consider application of species-specific toxicokinetic adjustments through the use of hemoglobin (Hb) adduct data.

EPA Response: As detailed in the revised metabolism section (Section 3.3) of the human health hazard assessment, available human hemoglobin adduct data for 1,3-butadiene have significant limitations that prevent their use for quantitative interspecies extrapolation. The revised Section 4.2.2.1 further clarifies that a well-defined MOA and robust mechanistic/toxicokinetic data are lacking for non-cancer effects other than ovarian toxicity. Additionally, high inter and intra individual variability, weak or inconsistent exposure response relationships, detectable background levels in unexposed populations, limited cohort diversity, and sex-dependent differences reduce confidence in species specific toxicokinetic adjustments based on these human Hb adduct data. According to EPA guidance for application of data derived extrapolation factors (DDEFs) (U.S. EPA, 2014), a DDEF requires: 1) sufficient information on an endpoint-specific mode of action, 2) data specific to the affected tissue, and 3) identification of the most appropriate dose metric. Because there is insufficient information to address the requirements, the agency has determined not to use Hb adduct data for deriving a data-derived extrapolation factor and instead relies on default dosimetric adjustments and uncertainty factors to account for interspecies differences and variability (for those endpoints and hazard values determined to be relevant to humans). Additional text has been added to the human health hazard assessment to address this consideration.

3.9.3 Comment

Summary: One commenter (0069) stated that the draft risk evaluation relies on a literature search that was conducted in 2019 and has not been updated since, except for when studies were identified in public comments or came to the attention of EPA staff, noting that the search strategy may not be comprehensive enough. It was suggested that EPA improve the data quality evaluation process by

including financial conflict of interest and implementing domain-based ratings instead of an overall quality determination.

EPA Response: In 2024, prior to completion of the *Draft Human Health Hazard Assessment* (U.S. EPA, 2024e), EPA updated the literature with studies published after September 2019 that informed important aspects of the human health assessment, including the cancer unit risk derivation and human health non-cancer dosimetry. In addition to building off the database from prior governmental assessments and supplementing with a complete systematic review of the literature through 2019, the Draft Human Health Hazard Assessment (U.S. EPA, 2024e) utilized both stakeholder comments and several rounds of literature searches to supplement the database with all reasonably available updated information informing 1,3-butadiene toxicokinetics, epidemiology, and dose-response assessment. These sources were then further supplemented by studies identified in public comments or by the SACC for the final *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d). Therefore, the final human health hazard and risk assessments are based on a comprehensive literature search and systematic review process, and EPA conclusions are based on the best available science.

EPA performs a robust systematic review of all data considered for the risk evaluation using consistent data evaluation criteria. The Agency carefully evaluates all assumptions and interpretations from submitted studies and does not rely on the interpretations of study authors. However, all data are given equal consideration and EPA applies the same rigorous process to all data sources regardless of financial interest. Data quality ratings are given both per domain and for the study as a whole.

3.9.4 Comment

Summary: One commenter (0069) asserted that EPA used deficient PECO (population, exposure, comparator, and outcome) inclusion criteria that excluded sub-organ level effects and stated that the 2021 systematic review protocol does not provide sufficient guidance for defining an apical effect. The commenter believed that EPA inappropriately excluded at least 37 PECO-relevant health studies through the further filtering process and others by rating them uninformative. Additionally, the commenter suggested that EPA uses inconsistent terminology between evidence synthesis and integration.

EPA Response: EPA did not exclude any studies through further filtering or data quality ratings. All of these studies were included in the hazard identification and evidence integration sections of the human health hazard assessment. While these studies were not the primary drivers of hazard values, they were still considered for their contribution to the overall weight of scientific evidence, provided they were generally valid. For instance, EPA discussed anemia findings from (Irons et al., 1986a, b), even though these studies did not pass the further filtering step. Additionally, histopathology of female reproductive organs from the study (Battelle PNL, 1982) was also considered in the weight of scientific evidence for that outcome.

As for excluding non-apical outcomes, EPA has not excluded any relevant health effects, and neither the SACC nor public commenters have provided evidence of missed endpoints or potentially increased risks from additional data sources. Sub-organ level effects including biochemical changes, cellular, and sub-cellular effects were considered in the Draft Human Health Hazard Assessment (U.S. EPA, 2024e). Specifically, EPA performed dose-response analysis on sub-organ level effects for hematological measurements indicative of anemia such as erythrocyte counts, hemoglobin concentrations, and cell volume. Adverse effects on sperm were also discussed in the hazard summary for male reproductive toxicity.

In reference to the comment about use of inconsistent terminology, EPA is now consistently using the term "evidence integration" instead of synthesis in the human health assessment to indicate developing weight of scientific evidence conclusions from the hazard database.

3.9.5 Comment

Summary: One commenter (0069) stated that EPA should publicly release the draft chemical-specific systematic review protocol before completing the draft risk evaluation as recommended by the Institute of Medicine and NASEM as a best practice. The commenter suggested that EPA consider issuing a new systematic review methodology document that updates how methods will be applied consistently across all TSCA risk evaluations.

EPA Response: EPA provided opportunities for public and SACC comment on the systematic review protocol for 1,3-butadiene as part of the draft risk evaluation package. EPA is using chemical-specific protocols to describe the updated processes for systematic review specific to each chemical, and any updates or modifications to EPA's approach are incorporated into the final risk evaluation package.

In general, EPA does not release a systematic review protocol prior to the draft risk evaluation because there are opportunities for public and SACC comment on the systematic review protocol as part of the draft risk evaluation package and in considering statutory deadlines for the risk evaluation process. As for a cross-cutting systematic review methodology document, EPA may release an update to the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021) after considering potential changes to the systematic review process for future chemical assessments.

3.9.6 Comment

Summary: One commenter (0080) commended EPA for updating the hazard endpoints for 1,3-butadiene and not relying on the 1982 IRIS value but suggests several refinements for EPA to consider. For the non-cancer risk assessment, this commenter (0080) supported the exclusion of the ovarian atrophy endpoint, the focus on fetal body weight changes, and EPA's conclusion to focus on repeated exposures. However, the commenter (0080) suggested that EPA review and apply the Mode of Action information for fetal body weight changes described in detail in Updated Hazard Assessment with Responses to EPA Questions; https://www.regulations.gov/comment/EPA-HQ-OPPT-2024-0425-0052, quantify and apply species differences in 1,3-butadiene metabolite internal dose, and evaluate recommendations from the independent review panel of MOA/Developmental toxicity/Dosimetry experts (A Manuscript Submitted for Publication (In Press): Human Health Risk Assessment for Exposures to 1,3-Butadiene in the United States with Input from an Independent Science Advisory Panel; https://www.regulations.gov/comment/EPA-HQ-OPPT-2024-0425-0052). The commenter (0080) went on to state the overall conclusion of the non-cancer analysis performed by the ACC Butadiene Panel.

EPA Response: The SACC also agreed with EPA's conclusions for ovarian toxicity.

EPA has reviewed the proposed mode of action (MOA) based on "general toxicity". In the revised Section 4.2.2.1 EPA determines that a well-defined MOA and robust mechanistic data are lacking for any non-cancer effect other than ovarian toxicity, and it is unknown whether a particular metabolite or set of metabolites are responsible for the observed critical outcomes. The cited document does not provide strong evidence to support species-specific toxicokinetic adjustments from the mouse data, and it even proposes "a plausible role for other BD metabolites, (including EB and EBD, the predominant epoxide metabolite BD estimated in humans)". Additionally, high inter and intra individual variability, weak or inconsistent exposure response relationships, detectable background levels in unexposed

populations, limited cohort diversity, and sex-dependent differences reduce confidence in species specific toxicokinetic adjustments based on available human Hb adduct data. The commenter appears to be recommending the use of a data derived extrapolation factor (DDEF) to adjust human equivalent concentrations/doses. According to EPA guidance for application of DDEFs (U.S. EPA, 2014), a DDEF requires: 1) sufficient information on an endpoint-specific mode of action, 2) data specific to the affected tissue, and 3) identification of the most appropriate dose metric. Because there is insufficient data across all these factors, the agency has determined not to use Hb adduct data for deriving a data-derived extrapolation factor and instead relied on default dosimetric adjustments and uncertainty factors to account for interspecies differences and variability. Additional explanation has been added to the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d) to address this consideration.

3.10 Potentially Exposed or Susceptible Subpopulations (PESS)

3.10.1 Comment

Summary: One public commenter (0088) stated that EPA failed to identify smokers and individuals with mEH gene polymorphism as potentially exposed or susceptible subpopulations, despite their greater exposure and susceptibility to 1,3-butadiene. Another commenter (0079) similarly noted that EPA does not quantify increased non-cancer risk for smokers, children, and elderly populations despite identifying these as PESS groups, and the default UF-H is insufficient for addressing risk to these groups with additional susceptibilities beyond the typical range of general population variability. A third group (0069) stated that EPA has not applied a consistent approach for identifying PESS in risk evaluations, and while the listing of PESS factors is a useful step, the evaluation of these factors is inconsistent and includes gaps.

EPA Response: EPA did identify both smokers and individuals with microsomal epoxide hydrolase mutations as a PESS group in Table 7-1 of the Draft Human Health Hazard Assessment (U.S. EPA, 2024e). This table has been included in all TSCA risk evaluations since 2021. As explained in Section 7.2 and Table 7-1 of that document, "for many factors EPA did not identify any reasonably available information to support quantitative adjustment of hazard/risk values". In accordance with guidance on data-derived extrapolation factors (DDEFs), EPA cannot apply additional uncertainty factors based on qualitative or non-specific evidence of susceptibility and must follow established EPA guidance. Adjustments to hazard values beyond the standard default factors must be based on sufficient quantitative data tied to a specific mode of action and target tissue (U.S. EPA, 2014). EPA's use of uncertainty factors is consistent with numerous EPA guideline documents (U.S. EPA, 2012a, 2002, 1994). EPA acknowledges that the lack of data covering specific susceptibilities is a limitation of the assessment in the *PESS Sensitivity* category of the Key Sources of Uncertainty in Section 6.1 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d). This table is also included in the final human health assessment.

3.10.2 Comment

Summary: Two public commenters (0105, 0069) noted that factors such as income inequality, violence, and healthcare inequity heighten susceptibility. A 42x intra-species adjustment factor was recommended for risk assessments (0122). Two commenters (0116, 0069) also recommend EPA apply additional adjustment factors to account for increased susceptibility of fenceline communities and other PESS groups experiencing extrinsic susceptibility factors.

EPA Response: In accordance with guidance on DDEFs, EPA cannot apply additional uncertainty factors based on qualitative or non-specific evidence of susceptibility and must follow established EPA

guidance. Adjustments to hazard values beyond the standard default factors must be based on sufficient quantitative data tied to a specific mode of action and target tissue (U.S. EPA, 2014). EPA's use of uncertainty factors (including the 10x intra-species factor for human variability) is consistent with numerous EPA guideline documents (U.S. EPA, 2012a, 2002, 1994). EPA acknowledges that the lack of data covering specific susceptibilities is a limitation of the assessment in the *PESS Sensitivity* category of the Key Sources of Uncertainty in Section 6.1 of the human health hazard assessment, and only if this data were reasonably available would the Agency be able to justify additional adjustment of hazard values for susceptible populations.

3.11 Cancer Assessment

3.11.1 Comment

Summary: Several comments (0105, 0116, 0069, 0125) questioned the 2024 IUR calculation due to reliance on potentially inaccurate exposure assessments with potential financial conflicts of interest. One commenter (0105) suggests using original exposure measurements for recalculation. One commenter (0069) stated that EPA used overestimated modeled exposure estimates by Macaluso 2004, which did not justify why modeled exposure estimates would be more reliable than NIOSH measurements. This commenter recommended that EPA calculate the IUR using original exposure information from the 2002 IRIS assessment that is based on measured data.

EPA Response: EPA disagrees that inaccurate exposure assessments were used. There are no "original" exposure measurements as suggested because the cancer cohort dates back to the 1940s and monitoring information is only available for a narrow window in the 1970s and 1980s. Macaluso 2004 represents the best available science given the need to estimate changing exposures across decades, including up to 30 years prior to the existence of any monitoring data (and prior to many modern exposure controls). NIOSH measurements do not align to the epidemiological data and do not cover the vast majority of the exposure period. As for conflict of interest, EPA performs a robust systematic review of all data considered for the risk evaluation using consistent data evaluation criteria. EPA carefully evaluates all assumptions and interpretations from submitted studies and does not rely on the interpretations of study authors. However, all data are given equal consideration and EPA does not apply a more or less rigorous process to one data source versus another.

3.11.2 Comment

Summary: Three commenters (0104, 0106, 0080) noted potential parameter inconsistencies in the life table calculation including lifetime, working years, exposure frequency and breathing rates. They suggested EPA adopt consistent parameter values for both life table calculations and exposure assessment to ensure accuracy. They also shared suggested parameter changes as well as changes to the life table calculations which would lead to lower risk for workers and the general population.

EPA Response: In response to this comment, additional details on exposure factors implemented into the lifetable analysis are described in Section 5.3.9.2 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d). Additionally, a new section providing a comparison between the assumptions and adjustments incorporated into the exposure and hazard values has been added in 5.3.1.3 of the risk evaluation.

Lifetables are an actuarial procedure to account for the dose-response effects of exposure over the lifetimes of a population in the presence of competing causes of death and account for the apportionment, an ever-smaller number of people in each increasing age category accordingly. They are used to transform occupational effect estimates to estimates suitable for general population unit risks.

The purposes of lifetable analysis and exposure assessment are different. Given the different purposes and objectives, some parameter values (*e.g.*, lifetime, working years, exposure frequency, and breathing rates), could be different to tailor to the specific purposes and populations. The selected parameters represent the best available science considering the reasonably available information while maintaining consistency with EPA guidance and other TSCA risk evaluations.

3.11.3 Comment

Summary: One commenter (0069) agreed with EPA's determination that 1,3-butadiene has a mutagenic mode of action and on inclusion of age-dependent adjustment factors; however, they suggested that an adjustment factor of 10 should also be applied to pregnant women and fenceline communities, citing a California EPA determination that an age sensitivity factor of 10 was also appropriate for the third trimester.

EPA Response: EPA recognizes that the commenter (0069) agrees with EPA's mutagenic mode of action and inclusion of age-dependent adjustment factors. EPA follows agency guidance in consideration and application of uncertainty and adjustment factors. Uncertainty factors are not applied to cancer risks, which conservatively use a linear slope down to zero and in the case of 1,3-butadiene also incorporate age-dependent adjustment factors to account for increased susceptibility of children. Both the IUR and lifetime exposure estimates are calculated starting at birth only. Including the third trimester in the adjusted period would not have a significant mathematical effect since it would be 3 months integrated into more than 78 years.

EPA does not apply an additional factor for pregnant women, and additional susceptibility factors beyond ADAFs are not applied to linear cancer values per EPA *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005a). Because EPA's Supplemental Guidance for Assessing Susceptibility from Early-life Exposure to Carcinogens (U.S. EPA, 2005b) explicitly excludes in utero exposure from quantitative ADAF adjustments, no additional 10-fold factor is applied for pregnant women or fetuses.

3.11.4 Comment

Summary: One commenter (0069) suggested that EPA should apply an additional adjustment factor for bladder and breast cancer. They state that the judgement of "indeterminate/no effect" for mammary tumors was based on a study with scientific issues and the animal data shows species concordance for mammary tumors. Bladder cancer findings were dismissed due to the absence of smoking data, but EPA was urged to reconsider this approach because 1,3-butadiene workers are not allowed to smoke in plants due to the chemical's explosive potential.

EPA Response: EPA has reviewed additional studies suggested by the SACC and continues to conclude that the overall human evidence for breast cancer is indeterminate because there was a lack of consistency in statistically significant effects across the available studies, demographics, and exposure levels. Bladder cancer has been combined with leukemia for the IUR in the final risk evaluation, so combined risk from both of those cancers is now accounted for.

3.11.5 Comment

Summary: For the cancer risk assessment, one commenter (0080) supported the use of styrene butadiene rubber (SBR) worker cohort data and the focus on the leukemia endpoint, but believes that EPA incorrectly attributed the slope value selected by EPA from Sathiakumar 2021 to the restricted cubic spline model instead of traditional modeling, that EPA used the incorrect percentile value calculated for UCL of slope (it was suggested to calculate the 95th percentile rather than the 97.5th

percentile), and that EPA's slope selection decision should include important covariates (*e.g.*, High Intensity Tasks or HITs).

EPA Response: In response to restricted cubic spline modeling, EPA has contacted the authors of the (Sathiakumar et al., 2021b) to confirm whether the cubic spline regression was used in the models that generated the β-coefficients. However, the authors did not respond to the EPA. To avoid confusion, "cubic spline regression" is removed from Table 5-8 and the context in Section 5.3.9.1.

With respect to the comment "percentile value calculated for UCL of slope," EPA agrees with the comment and is clarifying that the Agency relied on a one-sided 95 percent confidence bound in the IUR derivation. The reason for a one-sided bound is that in the BMD approach, the BMDL is derived by profile likelihood, and profile likelihood generally provides a one-sided interval. According to the EPA Benchmark Dose Technical Guidance (U.S. EPA, 2012b), BMDL or BMCL refers to the corresponding lower limit of a one-sided 95% confidence interval for the BMD or BMC, respectively.

Regarding the comment "EPA's slope selection decision," the slope is intended to estimate the association between 1,3-butadiene exposure and cancer. High-intensity tasks (HITs) signify the high exposure. Including HIT as a covariate can result in an over-adjustment of the association between 1,3-butadiene exposure and cancer.

3.11.6 Comment

Summary: Three commenters (0104, 0109, 0080) recommended that EPA rely on the full styrene-butadiene rubber (SBR) cohort data instead of a trimmed data set, which potentially overestimates the chemical's potency. They also recommended EPA use statistically significant covariates and correct descriptions of modeling techniques and suggested that EPA should correct the hazard value used for deriving inhalation unit risk through a lower benchmark response rate and reliance on a 90% confidence interval.

EPA Response: In response to relying on the full cohort data instead of a trimmed data set, since the purpose of the 1,3-butadiene IUR derivation is for 1,3-butadiene exposure and cancer, the models including unexposed people were not considered in EPA's evaluation Sections 5.3.9.1 and 5.3.9.5 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d) explain the reasons why EPA did not use the full cohort data set.

With respect to using statistically significant covariates, the statistical models and β-coefficients that EPA selected to present the dose-response relationships include covariates: age at hire, calendar year of hire, sex, race, plant, and payroll status (ever hourly paid or always salaried). These models were the best available science. EPA considered use of statistically significant covariates where appropriate. EPA did not use covariates that would have resulted in over-adjustment of the relationship between 1,3-butadiene exposure and the health outcomes.

EPA uses 1% as the benchmark response rate for most cancer sites based on biological and statistical considerations, as outlined in the EPA *Benchmark Dose Technical Guidance* indicated (U.S. EPA, 2012b), in response to the comment suggestion about correcting the hazard value. This rationale is described in Section 5.3.9.3.

EPA uses a one-sided 95 percent confidence bound, which is one of the bounds of two-sided 90 percent confidence interval, in response to the comment about deriving inhalation unit risk through the reliance on a 90 percent confidence interval. The reason for a one-sided bound is that in the BMD approach, the

BMDL is derived by profile likelihood, and profile likelihood generally provides a one-sided interval. According to the EPA BMDS Technical guidance, BMDL or BMCL refers to the corresponding lower limit of a one-sided 95 percent confidence interval for the BMD or BMC, respectively.

3.12 Human Health Risk Assessment

3.12.1 Comment

Summary: Three commenters (0087, 0109, 0069) suggested EPA use probabilistic modeling for more accurate risk estimates, including suggestions to follow the approach from the World Health Organization and identify an acceptable risk threshold across the population.

EPA Response: EPA is not using a probabilistic approach for calculating risk thresholds in risk evaluations under TSCA. EPA is currently in the early stages of researching the development of probabilistic methods and guidance for use in *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d). Until this research is matured and completed, EPA will continue to use the approaches described in existing EPA guidance documents for using default values (U.S. EPA, 2002) and for developing refined values (*e.g.*, 2014 Guidance for Applying Quantitative Data to Develop Data-Derived Extrapolation Factors for Interspecies and Intraspecies Extrapolation; (U.S. EPA, 2014)). There is no current policy for determining appropriate regulatory thresholds for results of a probabilistic analysis. Until probabilistic methods are standardized into guidance, the EPA does not wish to speculate on estimates of percent population affected.

3.12.2 Comment

Summary: One commenter (0109) recommended EPA should use average concentrations for cancer risk assessment because carcinogenic toxicity criteria are based on lifetime average exposures, making it representative of long-term contact concentrations.

EPA Response: EPA does use lifetime average daily concentration (LADC) for calculation of lifetime cancer risk. This has been consistently applied for all TSCA risk evaluations for evaluating risk using a linear-low-dose extrapolation approach. LADC averages exposures over a full lifetime and is inclusive of non-exposure times. EPA assumes a lifetime of 78 years on both the hazard derivation and exposure estimates, but in the case of 1,3-butadiene, the lifetable for derivation of the "adult-only" cancer unit risk was derived based on only 62 years of exposure, so the occupational risk calculations apply that same averaging time.

EPA assumes that by "average" the commenter means "central tendency". The risk determination for cancer did use central tendency exposure estimates because they represent more common exposure values which would be representative of long-term averages over a working lifetime.

3.12.3 Comment

Summary: One commenter (0110) provided exposure factors for intermediate exposure scenarios (*e.g.*, storage tank cleaning tasks). The commenter further recommended extrapolating the animal study exposure (*i.e.*, 10 days of exposure during 21-day gestation; ~50%) to the human gestation period to define intermediate exposure duration (*i.e.*, ~20 weeks) to ensure relevance and accuracy in findings.

EPA Response: This comment did not include a specific suggestion or context for what it would mean to extrapolate animal study exposure to human gestation. For intermediate scenarios, exposure is determined based on reasonable high-end assumptions of the number of working days for that occupational exposure scenario within a 30-day period (usually 22 days). Hazard endpoints are assigned

to intermediate scenarios when the endpoint requires multiple doses but less than chronic (10% of lifetime) exposure. EPA does not assume that exposure for 50% of the gestational duration is required for reduced fetal weight, as any repeated exposure during pregnancy would have a measurable effect on fetal weight.

EPA derives all non-cancer points of departure to a continuous basis, assuming exposure all day, every day, and generally uses the same exposure factors for all exposure scenarios and hazard derivations (exceptions are explained in Section 5.3.1.3 of the risk evaluation). This ensures consistency and more transparency by having a single set of hazard values and exposure defaults representing the chemical assessment. The risk calculations are then adjusted to be based on average exposures specific to the exposed populations and the relevant duration category (acute, intermediate, chronic). The risk evaluation covers all facilities in the United States, so standard assumptions must be used even if unique information is available for a single facility.

3.12.4 Comment

Summary: One commenter (0079) stated that EPA did not, but should have, modeled intermediate and acute exposures in the general population assessment to protect fenceline communities, especially from accidental, unplanned releases.

EPA Response: As stated in Section 4.2.2.3.1 of the human health hazard assessment, it is unlikely any adverse effects will result following a single exposure at concentrations relevant to human exposures (*e.g.*, below the OSHA STEL). Therefore, the Agency did not derive an acute non-cancer hazard value for risk estimation because any options would have low confidence and would be less protective than the intermediate POD or existing regulatory limits. Acute exposures are not of concern because there is no relevant hazard outcome expected. As for intermediate exposures, EPA has not identified reliable approaches for estimating intermediate exposures for the general population because releases are reported as yearly values and there is insufficient information available to determine the relative proportion of releases or resulting exposures occurring over an intermediate period (*e.g.*, one month).

3.12.5 Comment

Summary: One commenter (0079) stated that the use of [the Integrated Indoor-Outdoor Air Calculator] (IIOAC) modeling was flawed because it "is a narrower model" and does not aggregate risks from multiple neighboring facilities. It additionally does not consider exposures less than 100m or greater than 1000m from a facility while HEM includes distances as close as 10m and as high as 50 km. Both IIOAC and HEM use AERMOD, so EPA should just use HEM as a first step because it can aggregate across multiple sources and has a wider range of distances that can be considered.

EPA Response: IIOAC is used primarily as an initial screening. EPA proceeds with the more resource-intensive HEM to further refine modeling concentrations, aggregate risk estimates, and quantify the impacted population. This tiered approach is detailed in the final risk evaluation.

3.13 Aggregate Exposures and Cumulative Risk

3.13.1 Comment

Summary: One public commenter on the 2018 docket (EPA-HQ-OPPT-2018-0451-0060) and several commenters on the 2024 docket (EPA-HQ-OPPT-2024-0425-0088, 0105, 0116, 0069, 0079, 0092) noted that EPA underestimated risks by not adequately considering aggregate and cumulative exposures, including those from multiple facilities, unintended releases, and background sources like vehicle exhaust and tobacco smoke. One public commenter (0092) noted that EPA's supplement does not

account for aggregate exposures from multiple facilities, potentially underestimating real-world cancer risks. For example, two facilities in Orange, TX were analyzed separately, ignoring the combined exposure from multiple nearby emitters. One commenter (0079) also suggested aggregating across exposure sources such as occupational, background, and from fenceline exposure for those who may be part of multiple PESS groups.

EPA Response: The final risk evaluation aggregates exposures for estimation of both non-cancer and cancer risks (Section 5.3.4, 5.3.5, and 5.3.6). TSCA statute does not require EPA to conduct cumulative risk assessments, although the Agency may complete cumulative assessments on a chemical-specific basis when the best available science indicates that it is an appropriate course. EPA is not performing a cumulative risk assessment for 1,3-butadiene as part of this risk evaluation (See comment 3.13.2). The Agency notes that a *Draft Proposed Approach for Consideration of Chemical Co-exposure in TSCA Risk Evaluations* was peer-reviewed in 2024 and may inform future risk evaluations (U.S. EPA, 2024b). The exposure assessment considered monitoring information including for ambient air outside of facilities that use 1,3-butadiene in conjunction with modeled exposures for the general population based on reported releases from industrial sites (*General Population Exposure for 1,3-Butadiene* Section 2.3.1 (U.S. EPA, 2025c)). EPA did qualitatively consider and contextualize multiple sources of 1,3-butadiene, including automobile exhaust (onroad and nonroad mobile sources), residential wood burning, natural fires through the AirToxScreen discussion in Section 2.3.2.2 of the *General Population Exposure for 1,3-Butadiene* (U.S. EPA, 2025c). Thus, measured background concentrations were considered as part of the body of evidence for general population exposures to 1,3-butadiene including as context for measured and modeled concentrations that were directly related to TSCA conditions of use.

3.13.2 Comment

Summary: Multiple commenters (0079, 0069, 0088, 0105, 0116) stated that EPA should consider cumulative risks from co-exposure to similar chemicals such as formaldehyde given the shared health outcomes and likely co-exposure. This is especially important because 1,3-butadiene can degrade to formaldehyde and acrolein in the atmosphere. An additional adjustment factor could be added to account for cumulative risks for chemicals with common adverse outcomes.

EPA Response: Data evaluated by EPA suggest that localized formation of the major transformation products from 1,3-butadiene, formaldehyde and acrolein, would not lead to a sustained or measurable increase in ambient concentrations beyond existing background levels. Therefore, secondary formation of formaldehyde and acrolein is not anticipated to significantly impact exposure or alter risk conclusions. Therefore, these specific compounds will not be included in the risk assessment. There are three major reasons for this. Firstly, formaldehyde and acrolein are not uniquely attributable to 1,3-butadiene, as emissions from TSCA-regulated sources and other natural and anthropogenic activities, such as vehicle exhaust and secondary formation from other VOCs, far exceed the quantities that could reasonably be formed through atmospheric degradation of 1,3-butadiene released form TSCA facilities. Consequently, any incremental contributions from 1,3-butadiene photodegradation would be negligible relative to environmental releases and background levels of formaldehyde (U.S. EPA, 2024a), rendering formaldehyde as a 1,3-butadiene degradate immaterial to the risk characterization. Second, the atmospheric photodegradation of 1,3-butadiene involves complex radical-mediated pathways that are influenced by local photochemical conditions, including ambient concentrations of relevant radicals, sunlight intensity, temperature, and the presence of co-pollutants (Khaled et al., 2019; Vimal, 2008; Andersson and Ljungström, 1989). Any model-based estimation would entail considerable uncertainty and offer limited value for risk assessment purposes. Third, both formaldehyde and acrolein undergo rapid photodegradation in the atmosphere, with half-lives typically measured in hours. Due to this rapid degradation, these compounds do not persist or accumulate in the environment.

The Agency notes that a *Draft Proposed Approach for Consideration of Chemical Co-exposure in TSCA Risk Evaluations* was published and peer-reviewed in 2024 and may inform future risk evaluations (U.S. EPA, 2024b).

3.14 Risk Determination

3.14.1 Comment

Summary: Two public commenters (0085, 0068) expressed disagreement for EPA's "whole chemical approach," specifically, the decision to make a single risk determination for a chemical substance rather than making separate determinations for each COU. One commenter (0085) stated that the single risk determination approach reduces clarity and certainty provided by the previous approach of making separate determinations of unreasonable risk for every condition of use of a chemical and that the consequences of the whole chemical approach have resulted in prolonged uncertainty for the regulated community, continued use of resources to research uses which pose no risk, and a negatively biased whole chemical "finding" that will undoubtedly be used to push back on uses that may not have an unreasonable risk. They note that the whole chemical approach may also potentially result in regrettable substitutions, as manufacturers seek to quickly implement functional alternatives. Whereas another commenter (0088) agreed that EPA "…correctly finds that 1,3-butadiene, as a whole chemical…," presents unreasonable risk.

EPA Response: EPA conducted the risk evaluation of 1,3-butadiene according to the current TSCA risk evaluation framework rule, which requires EPA to make a single risk determination on a chemical substance. See 40 CFR §702.39(f)(1); see also 87 Fed. Reg. 37028 (May 3, 2024). TSCA section 6(b)(4)(A) specifies that a risk evaluation must determine whether "a chemical substance" presents an unreasonable risk of injury to health or the environment "under the conditions of use." In evaluating 1,3-butadiene's risk, the Agency considered exposures associated with each condition of use, but did not make separate risk determinations. A single determination that a chemical substance presents an unreasonable risk does not mean that the entirety or whole of that chemical's uses – or even a majority of uses – presents an unreasonable risk. The 1,3-butadiene Final Risk Evaluation considered the chemical's COUs (*i.e.*, the intended, known and reasonably foreseen circumstances under which the chemical is manufactured, processed, distributed in commerce, used or disposed of). The potentially different exposure scenarios presented by different COUs are reflected in the risk evaluation's exposure assessment. In the 1,3-butadiene final risk evaluation, EPA listed the COUs that significantly contribute to the unreasonable risk, and any future risk management rule will likely focus on those COUs.

EPA has published a proposed rule outlining changes and revisions to the current regulations to effectuate the best reading of the statute and to ensure the timely completion of risk evaluations and effective and efficient protection of health and the environment. See 90 Fed. Reg. 45690 (September 23, 2025). However, this final risk evaluation (including its risk determination and the identification of significant contributors to the unreasonable risk) provides ample basis and clarity to support appropriate risk management rulemaking, consistent with the statute.

3.14.2 Comment

Summary: One commenter (0083) stated that importing should be evaluated separately from manufacturing due to differences in activities and exposures. The commenter (0083) agreed with EPA that it is more appropriate to evaluate occupational exposures under the importing category separately from occupational exposures for manufacturing, noting that the activities, number of workers, exposure

frequencies, and exposure durations are very different between the two categories. The commenter however notes that putting importing back into the manufacturing category to make a single determination that covers both uses is confusing and should be reconsidered.

EPA Response: In EPA's draft risk evaluation for 1,3-butadiene and in the final risk evaluation, the subcategories "domestic manufacturing" and "importing" are counted as separate COUs and the determination differentiates between these activities. To clarify, TSCA defines "manufacture" to mean "import into the customs territory of the United States (as defined in general note 2 of the Harmonized Tariff Schedule of the United States), produce, or manufacture" (TSCA §2602). So, although "import" falls under the definition of "manufacturing" and is therefore under the larger COU life cycle stage of "manufacturing," the determination considers domestic manufacturing and import separately.

3.14.3 Comment

Summary: Two commenters (0085, 0068) recommended that EPA incorporate standard industry safety practices, as reflected in Material Safety Data Sheets and OSHA requirements, into its risk assessment of 1,3-butadiene and other TSCA chemicals, stating that assuming no use of PPE in any workplace will likely overestimate worker exposure. One commenter (0085) stated that, because of this, the risk determinations may be "inaccurate and misleading and result in extra workload and resources for EPA and the regulated community alike going into the risk management phase." They (0085) further stated that waiting until EPA proceeds to the risk management phase to include the use of OSHA-required PPE and related workplace standards "creates a false impression of risk that lacks transparency, will be misleading to the public, and overestimates the risk of exposure in workplaces that require workers to follow PPE practices." Another commenter (0068) stated "a chemical should not be regulated in an industrial or commercial setting where it is contained in a closed loop system or where strict personal protective equipment (PPE) and industrial controls are in place that already manage the unreasonable risk posed by the chemical."

EPA Response: All risk evaluations to date, including the 1,3-butadiene Final Risk Evaluation, have considered PPE in occupational settings, including in the occupational exposure assessment where PPE is considered in the exposure scenarios. Additionally, when the Agency receives information demonstrating the use of PPE and what types, it can be used to inform EPA's risk evaluation so that it can reflect real working conditions which can be incorporated into the exposure scenarios. In determining whether unreasonable risk is presented, EPA's consideration of occupational exposure scenarios took into account reasonably available information on the implementation and use of occupational exposure control measures such as engineering and administrative controls and PPE. Regarding the use of PPE, as discussed in Section 7.1.3 of the risk evaluation, the American Chemistry Council (ACC) 1,3-butadiene TSCA Risk Evaluation Consortium (Consortium) provided information regarding the use of respirators. The information indicates that respirators tend to be used for all tasks, with types varying depending on the task and air concentrations measured. Specifically for short term exposures, the Consortium data indicate some type of respiratory protection is used for every task activity where 1,3-butadiene exposure might exceed the OSHA PEL occur. While there is evidence that PPE is worn, it is uncertain how consistently that is occurring at all facilities and for the entirety of the task/exposure duration. Based on this information, described exposures, that may occur and result in unreasonable risk in domestic manufacturing facilities, are not necessarily being addressed through existing PPE practices. While EPA provided risk estimates with the level of PPE (up to a maximum of

APF 50) that would mitigate the unreasonable risk if applied, EPA based its risk determination on risk estimates without PPE.

3.14.4 Comment

Summary: One commenter (0082) sought clarification on whether the use of synthetic rubber in tire manufacturing contributes significantly to the overall unreasonable risk finding. The commenter (0082) stated that "the commercial use of synthetic rubber to manufacture rubber tires is synonymous with and encapsulates the "rubber compounding" and "rubber converting" OESs," further stating that "it makes no sense for EPA to conclude that the commercial use of synthetic rubber does not contribute significantly to the overall unreasonable risk finding and conclude that the "rubber compounding" and "rubber converting" OESs do contribute[to the unreasonable risk]."

EPA Response: EPA has determined that the COUs associated with plastics and rubber compounding and converting, which includes incorporation of synthetic rubber into articles like tires, significantly contribute to the unreasonable risk of 1,3-butadiene. See Section 7 of the Risk Evaluation. EPA's risk estimates for these uses are based on 53 8-hour worker samples relevant to plastics and rubber compounding, 50 8-hour samples relevant to plastics and rubber converting, and 44 12-hour samples used for both. The commercial use of already manufactured tires (*i.e.*, Commercial use – Synthetic rubber) does not significantly contribute to the unreasonable risk.

3.14.5 Comment

Summary: One commenter (0088) stated that "EPA's reliance on central tendency risk estimates violates TSCA's mandate to evaluate and eliminate 1,3-butadiene's unreasonable risks to potentially exposed or susceptible subpopulations" and that it is inconsistent with longstanding EPA practice and is arbitrary and capricious. The commenter went on to state that "the 95th percentile exposure level for a given condition of use does not necessarily reflect a peak exposure level that all workers experience on rare occasions. Instead, it is more likely to represent the exposures that subset of workers in higher risk jobs or workplaces experience every day." Another commenter (0105) noted that although EPA's analysis supports the conclusion of unreasonable risks to workers, it underestimates those risks by using central tendency for chronic scenarios. They recommend that high-end exposures should be used consistently. Other commenters (0116, 0069, 0122) believed the EPA's determination of unreasonable risk to workers is flawed because it relies on central tendency estimates instead of high-end exposure estimates, overlooking risks to workers who experience higher-than-average exposures. The approach should consider exposure variability across workplaces, as different procedures can lead to consistent day-to-day concentration differences.

EPA Response: The use of either central tendency or high-end risk estimates to make a determination of unreasonable risk is based on considerations of the reasonably available information about a typical scenario and process within the COU for a particular chemical, information about PESS groups, and other risk-related factors. In past EPA risk evaluations, where EPA did not have specific PESS data, the Agency relied on high-end or conservative exposures for all scenarios to account for risk to PESS populations. However, because reasonably available monitoring data are incorporated in the 1,3-butadiene assessment, exposure estimates based on inputs and scenarios that are most representative and/or are likely to occur do incorporate PESS considerations. For the 1,3-butadiene risk evaluation, EPA was able to incorporate considerations for multiple PESS factors into risk estimates, as presented in Section 5.3.5. EPA made risk determinations based on the most appropriate, conservative assumption of a worker's exposure level over the relevant exposure duration. EPA agrees that high-end exposures may be experienced for multiple days or weeks, which is applicable to intermediate exposures. However, it is not likely that a worker is experiencing the highest percentile of exposure every day for their entire 40-

year career, which is the averaging time relevant to chronic exposure. In addition, EPA incorporated inhalation monitoring data to estimate central tendency and high-end worker inhalation exposures. In the final risk evaluation, EPA included in the risk characterization its assessment of whether central or high-end exposure estimates are reflective of worker exposures based on available information, including information about shift duration, frequency, and intensity of exposures.

3.14.6 Comment

Summary: One commenter (0079) proposed using the more protective 1×10^{-6} benchmark for all populations, as opposed to having a less protective benchmark for workers of 1×10^{-4}.

EPA Response: EPA relied on NIOSH guidance (Whittaker et al., 2016) when choosing the 10^{-4} cancer risk benchmark to evaluate risks to workers from 1,3-butadiene exposure. NIOSH's mandate, on pg. iii of Whittaker et al. (2016), is to: "… describe exposure levels that are safe for various periods of employment, including but not limited to exposure levels at which no employee will suffer impaired health or functional capacities or diminished life expectancy as a result of his work experience." Although NIOSH guidance, p. 20, states that: "exposures should be kept *below* a risk level of 1 in 10,000, *if practical* [emphasis added]" EPA uses the 1 in 10,000 benchmark during the risk evaluation stage for TSCA chemicals for workers. It is important to note that 1×10^{-4} is not a bright line, and EPA has discretion to make unreasonable risk determinations based on other benchmarks or factors as appropriate. See Section 5.1.1.2 of the Risk Evaluation for additional information. EPA has consistently applied a cancer risk benchmark of 1×10^{-4} for assessment of occupational scenarios under TSCA. For cancer risk assessments for the general population, EPA and other regulatory agencies, often consider an increased cancer risk above benchmarks ranging from 1 in 1,000,000 to 1 in 10,000 (*i.e.*, 1×10^{-6} to 1×10^{-4}) depending on the subpopulation exposed. EPA provides discussion of the risks to the general population, and how the cancer risks in, above, and below this range were considered in Sections 5.3.4 and 5.3.5 of the risk evaluation. This discussion includes consideration of PESS.

3.15 Other Topics

3.15.1 Comment

Summary: One commenter (0053) noted that the U.S. National Institute for Occupational Safety and Health (NIOSH) recognizes that there is no safe level of exposure to a carcinogen, and quotes NIOSH stating that "reduction of worker exposure to chemical carcinogens as much as possible through elimination or substitution and engineering controls is the primary way to prevent occupational cancer." This commenter (0053) also stated that ECHA considers no butadiene health-based occupational exposure limit (OEL) nor that a short-term exposure limit (STEL) can be identified. Instead, ECHA Risk Assessment Committee derived an exposure-risk relationship expressing the excess cancer risk as a function of the air concentration of 1,3-butadiene (ECHA 2024).

EPA Response*:* EPA appreciates the commenter providing this information.

3.15.2 Comment

Summary: One commenter (0053) stated that more research on 1,3-butadiene risk is needed in certain environments containing cigarette smoke, as well as the potentially harmful butadiene metabolites found in cigarette smokers. The commenter (0053) referenced findings from the International Agency for Research on Cancer which has classified 1,3-butadiene as a human carcinogen and provides data for 1,3-butadiene exposure in the U.S. population, stating that tobacco smoke is a major exposure source. The

commenter (0053) also stated that 1,3-butadiene is considered "the most carcinogenic compound in cigarette smoke."

EPA Response: TSCA section 3(2)(B), which defines "chemical substance," excludes "tobacco or any tobacco product." According to section 201 of the Federal Food, Drug, and Cosmetic Act (FFDCA), "tobacco product" means "any product made or derived from tobacco that is intended for human consumption, including any component, part, or accessory of a tobacco product." 21 U.S.C. §321(rr)(1). Section 900(3) of the FFDCA establishes that a "cigarette" is "a product that . . . is a tobacco product . . . and . . . includes tobacco, in any form, that is functional in the product, which, because of its appearance, the type of tobacco used in the filler, or its packaging and labeling, is likely to be offered to, or purchased by, consumers as a cigarette or as roll-your-own tobacco," and section 901(b) of the FFDCA makes clear that FDA has authority over "all cigarettes, cigarette tobacco, roll-your-own tobacco, and smokeless tobacco." 21 U.S.C. §§387(3) and 387a(b). EPA thus determined that a "cigarette" is a "tobacco product," and, therefore, is not a "chemical substance." Similarly, EPA determined that "tobacco" is not a "chemical substance." Therefore, EPA cannot assess tobacco or cigarettes as a COU of the chemical substance nor issue a rule pursuant to TSCA section 6(a) to apply requirements to tobacco or cigarettes.

3.15.3 Comment

Summary: One commenter (0081) stated that they do not have any comments on the risk evaluation but provided feedback in advance of the risk management process on aerospace and defense COUs, particularly those deemed critical.

EPA Response*:* EPA will consider the information provided as we move into the risk management process.

3.15.4 Comment

Summary: One commenter (0085) noted 1,3-butadiene's role as a "building block chemical," and expresses concern over how unreasonable risk finding for 1,3-butadiene will impact those downstream production processes and uses. The commenter (0085) stated that EPA "may create a set of unintended consequences that could result in major supply and economic impacts on a wide array of industrial sectors and products, none of which are recognized in this draft risk evaluation." The commenter (0085) stated that the evaluation must "identify all the downstream uses and be transparent as to how an unreasonable risk determination would impact them."

EPA Response: EPA lists the conditions of use (COUs) and describes the life cycle stages, categories, and subcategories that comprise TSCA COUs which EPA assessed in its final risk evaluation in Section 2.2 of the document. These COUs include the downstream products and articles mentioned by this commenter and others, which may only contain trace amounts of 1,3-butadiene. Any impacts that could result from regulation of either the upstream or downstream uses of 1,3-butadiene would be analyzed and considered during the risk management phase.

3.15.5 Comment

Summary: Several commenters (0067, 0068, 0077, 0080, 0081, 0085, 0109, 0115) recommended that EPA derive, establish, and publish a de minimis concentration limit (threshold of regulatory concern) for all downstream products and articles, noting that most specification qualified products appear to contain trace amounts (less than 0.1%) of 1, 3-butadiene. Commenters requested that as EPA develops a risk management rule for 1, 3-butadiene, it considers including a regulatory threshold below which 1, 3-butadiene usage will be deemed not to violate the rule. One commenter (0077) encouraged the inclusion

of a de minimis level for 1,3- butadiene and stated that it will enable manufacturers and processors to conduct appropriate due diligence regarding residuals and byproducts while addressing the risk considerations of 1,3-butadiene. Commenters noted that disclosure at the 0.1 percent threshold is also consistent with OSHA's Hazard Communication Standard requirements, stating that aligning these requirements would assist the industry, particularly downstream users, in readily determining and ensuring compliance with their obligations under TSCA.

EPA Response: EPA appreciates the comments regarding uses where trace amounts of 1,3-butadiene may be present. However, establishing a regulatory threshold level for 1,3-butadiene would be considered during EPA's risk management of the unreasonable risk identified for TSCA COUs and is therefore not discussed in EPA's final *Risk Evaluation for 1,3-Butadiene* (U.S. EPA, 2025g).

3.15.6 Comment

Summary: For workers not covered by OSHA standards, one commenter (0085) recommended that EPA work with OSHA to find an appropriate means for providing any necessary requirements, preferably under the Occupational Safety and Health (OSH) Act, if unreasonable risk is determined. Further, if EPA believes that certain workplace risks are not being adequately controlled, then the commenter (0085) stated that EPA has an obligation under TSCA section 9(a) to consult with OSHA before superseding OSHA authority, and that any such result from coordination and consultation with OSHA should be made publicly available to further transparency, process, and due diligence.

EPA Response: TSCA provides EPA with the authority to regulate chemicals determined to cause unreasonable risk. EPA is coordinating with federal partners, including OSHA and NIOSH, to promote consistency, transparency, and easier implementation of any regulations affecting the chemical industry.

3.15.7 Comment

Summary: A public commenter (0058) requested that EPA allow the continued manufacture and import of 1,3-butadiene materials until alternatives are developed and qualified. They also requested that EPA permit processing and distribution of these materials until the end of their service life as well as enable continued use at nuclear facilities until the end of the material's service life.

EPA Response: Thank you for your comment. EPA will address the manufacture, import, processing, and distribution of 1,3-butadiene during risk management under TSCA section 6(a).

3.15.8 Comment

Summary: One public commenter (0117) made the following requests of EPA related to risk evaluations in general:

- Make risk and hazard information publicly available in stakeholder-accessible language and transparently describe baseline assumptions, reasoning, and data underlying regulatory decisions.
- Encourage the standardization and harmonization of hazard criteria and risk assessment language to ensure all parties use a common global vocabulary.
- Include considerations for vulnerable and marginalized populations in risk management decisions, ensuring their protection.
- Adopt a framework for risk-based decision-making and support the development and use of less toxic and less persistent chemicals, as well as alternatives assessment processes.
- Utilize best practices for modeling and assessment, including robust exposure data, to understand chemical uptake by vulnerable populations.
- Use biomonitoring to evaluate the environmental and health implications of chemical exposure and the success of sustainable molecular design and safer alternatives. Develop alternative and

more efficient means of toxicity testing to minimize the use of vertebrate animals in chemical testing.

- Encourage government agencies to adopt a tiered approach to risk assessment that incorporates NAMs, analog data, and validated animal alternatives when necessary, ensuring transparency in baseline assumptions and data requirements.
- Encourage agencies to have clear operational mandates to minimize overlap in responsibilities.

EPA Response: EPA follows the statutory requirements of TSCA and the procedures of the Risk Evaluation Rule when determining what chemicals to assess, how to perform those assessments, and how to regulate potential unreasonable risk. Any additional activities are not statutorily mandated and are outside the scope of the review of this risk evaluation. As required by the TSCA statute and risk evaluation rule (EPA-HQ-OPPT-2025-0260), EPA publishes the results of systematic review, including data extraction and data quality evaluation findings, as well as a risk evaluation and technical support documents for each high-priority substance including 1,3-butadiene. These documents outline the information, approaches, and assumptions used in assessment of risk for each condition of use that is in-scope. Further, the Agency publishes a nontechnical summary of the risk evaluation at the time that the final risk evaluation is published. EPA will consider working with standardized hazard criteria and language in risk evaluation and communication and may adopt such approaches only to the extent that they align with the statute and implementing rules. Risk management, including alternatives assessment, is a later stage in the process and out of scope for finalization of the risk evaluation package. TSCA charges the Agency with assessing and, as appropriate, regulating substances to mitigate risks, and other statutes and programs at EPA are oriented toward encouraging the development and use of alternative chemicals. EPA uses robust, peer-reviewed approaches in TSCA risk evaluations which rely on both modeled and measured information, to assess risks to populations including Potentially Exposed and Susceptible Subpopulations (PESS) as required by the statute. Biomonitoring is among the types of data that EPA uses in TSCA risk evaluations when that information is available and was used in the risk evaluation for 1,3-butadiene to compare human and rodent metabolism. The TSCA statute directs EPA to reduce the use of vertebrates in chemical testing and to promote the development and use of alternative testing methods, or New Approach Methodologies (NAMs). The Agency's to Strategic Plan to Promote the Development and Implementation of Alternative Test Methods has been published.[2] EPA contributes to inter-agency work groups and communities of practice to communicate with federal partners about developments and lessons learned in risk assessment.

3.15.9 Comment

Summary: A public commenter (0059) advocated for a ban on 1,3-butadiene considering the unreasonable risk to human health when working with 1,3-butadiene and prevalence in the environment.

EPA Response: EPA has determined that 11 COUs significantly contribute to the unreasonable risk of 1,3-butadiene and will initiate risk management for 1,3-butadiene by applying one or more of the requirements under TSCA section 6(a) to the extent necessary so that 1,3-butadiene no longer presents an unreasonable risk.

3.15.10 Comment

Summary: A public commenter (0125) submitted a correction to the scientific conversation on Day 3 of the 1,3-butadiene SACC, April 3, 2025. The commenter clarified that the American Chemistry Council (ACC) is not the owner of human health outcome data for the SBR cohort; The data are owned by the International Institute of Synthetic Rubber Producers (IISRP), which submitted it to the EPA on October

[2] https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/strategic-plan-reduce-use-vertebrate-animals-chemical

17, 2023. The commenter further clarified that ACC did not request a 45-minute time slot for the hazard assessment presentation but rather was advised that EPA would recommend a 45-minute allowance to SACC. This public comment included additional discussion of human exposure estimates and toxicokinetic data from workers, combined cancer risk, and flaring operations.

EPA Response: EPA confirms that, in response to EPA's Summer 2023 request for model inputs used to derive a cancer potency value (IUR) in Valdez-Flores 2022 (Valdez-Flores et al., 2022), IISRP did provide raw exposure and outcome data underlying the IUR derivation. These data were submitted via CDX and received in October 2023.

EPA has a long-standing process for the public who would like to make oral comments during peer review meetings to send a request and/or a written version of an oral presentation. EPA received requests for oral comments and considered and granted additional time for speakers who requested more time within the constraints of the agenda to address the agency's charge questions. EPA continues to value the feedback, input and data that the agency may consider in reviewing risk evaluation such as in this case for the 1,3-Butadiene undergoing risk evaluation under the Toxic Substances Control Act. EPA clarifies that the entire history of the SBR cohort reporting used modeled data to estimate worked exposure. In 2004, Macaluso updated their own modeling from the 1990s using additional interviews and data collection to refine the historical estimates (Macaluso et al., 2004; Macaluso et al., 1996). Monitoring data connecting exposures and outcomes among individual participants is not available. Modeling is required because the cohort exposure duration is 1943-1992; NIOSH monitoring reported in Fajen et al., 1990 surveys years 1984 through 1987 (Fajen et al., 1990). Exposures prior to the 1970s are estimated to be much higher than modern exposures due to the advent of engineering controls and establishment of OSHA, NIOSH and standardized detection methods. The NIOSH monitoring data were used to support the Macaluso model derivation. Notably, Sathiakumar et al., 2007 found that Macaluso et. al., (2004)-modeled estimates at one Canadian SBR plant were similar or *lower* than monitored measurements from the matched time period and job series (Sathiakumar et al., 2007). No previous dose-response assessments (*i.e.*, neither Health Canada 2000 nor EPA 2002) have used NIOSH monitored data as the sole basis of exposure assessment; all dose-response studies (which lay foundation for the IUR) have relied on modeled data extending back to 1943, the start of the styrene-butadiene rubber (SBR) cohort. EPA notes that all, but one, 1,3-butadiene occupational exposure assessment publications are supported by industry (*e.g.*, IISRP). The single exception is the 3-year (1984-1987) NIOSH survey of monitored exposure published by Fajen et al. (Fajen et al., 1990). Discussion of the cancer exposure assessment can be found in Section 5.4 of *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d).

Consideration of human toxicodynamics, including hemoglobin adduct data, is reflected in Section 3.3 and Table 7-17 of the *Human Health Hazard Assessment for 1,3-Butadiene* (U.S. EPA, 2025d). Bladder cancer was combined with leukemia to derive cancer risk in the 1,3 Butadiene Risk Evaluation. Additional cancer types were considered and discussed in Section 5.1 of the *Human Health Hazard Assessment* (U.S. EPA, 2025d) but were not combined with bladder cancer and leukemia. Reported emissions were modeled in HEM and presented in the 1,3-Butadiene Risk Evaluation (U.S. EPA, 2025g). Specifically, NEI, which included emissions from flaring, was used to refine risk estimates in Section 2.2 of *General Population Exposure for 1,3-Butadiene* (U.S. EPA, 2025c).

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