United States
Environmental Protection Agency

Office of Chemical Safety and
Pollution Prevention

Summary of External Peer Review and Public Comments and Disposition for Trichloroethylene (TCE)

Response to Support Risk Evaluation of Trichloroethylene (TCE)

November 2020

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

EPA appreciates the valuable input provided by the public and peer review panel. The input resulted in numerous revisions to the hazard summary.

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

1. Environmental Fate and Exposure
2. Environmental Exposure and Releases
3. Environmental Hazard
4. Occupational and Consumer Exposure
5. Human Health Hazard
6. Risk Characterization
7. Overall Content and Organization

All peer review comments for the seven charge questions are presented first, organized by charge question in the following section. These are followed by the public comments. For each theme, general comments are presented first, and then additional comments follow.

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

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List of Comments		
#	Docket File	Submitter
31	EPA-HQ-OPPT-2019-0500-0031	Anonymous
32	EPA-HQ-OPPT-2019-0500-0032	Anonymous
33	EPA-HQ-OPPT-2019-0500-0033	ToxStrategies
34	EPA-HQ-OPPT-2019-0500-0034	Anonymous
35	EPA-HQ-OPPT-2019-0500-0035	Anonymous
36	EPA-HQ-OPPT-2019-0500-0036	W. Germann
37	EPA-HQ-OPPT-2019-0500-0037	Jennifer McPartland, Senior Scientist, Environmental Defense Fund (EDF)
38	EPA-HQ-OPPT-2019-0500-0038	Anonymous
39	EPA-HQ-OPPT-2019-0500-0039	Anonymous
44	EPA-HQ-OPPT-2019-0500-0044	Richard A. Denison, Lead Senior Scientist, EDF
45	EPA-HQ-OPPT-2019-0500-0045	Anonymous
47	EPA-HQ-OPPT-2019-0500-0047	Michelle Roos, Environmental Protection Network (EPN)
48	EPA-HQ-OPPT-2019-0500-0048	Exponent, Inc. on behalf of the American Chemistry Council and the Halogenated Solvents Industry Alliance
49	EPA-HQ-OPPT-2019-0500-0049	Liz Hitchcock, Director, Safer Chemicals Healthy Families (SCHF) et al.
50	EPA-HQ-OPPT-2019-0500-0050	Suzanne Hartigan, Senior Director, Regulatory and Technical Affairs, American Chemistry Council (ACC)
51	EPA-HQ-OPPT-2019-0500-0051	Stephen P. Risotto, Senior Director, ACC
52	EPA-HQ-OPPT-2019-0500-0052	ToxStrategies on behalf of the ACC
56	EPA-HQ-OPPT-2019-0500-0056	Richard A. Denison, Lead Senior Scientist, EDF
57	EPA-HQ-OPPT-2019-0500-0057	Richard A. Denison, Lead Senior Scientist, EDF
58	EPA-HQ-OPPT-2019-0500-0058	Jennifer Sass, Senior Scientist, Natural Resources Defense Council (NRDC)
60	EPA-HQ-OPPT-2019-0500-0060	Daniele Wikoff, Health Sciences Practice Director, ToxStrategies
61	EPA-HQ-OPPT-2019-0500-0061	David Michaels, Department of Environmental and Occupational Health, Milken Institute School of Public Health, The George Washington University
62	EPA-HQ-OPPT-2019-0500-0062	I. Rusyn
63	EPA-HQ-OPPT-2019-0500-0063	James Bus, Toxicologist, Exponent, Inc. for the Halogenated Solvents Industry Alliance (HSIA)
64	EPA-HQ-OPPT-2019-0500-0064	Jennifer Sass, Senior Scientist, NRDC
65	EPA-HQ-OPPT-2019-0500-0065	Lindsay McCormick, EDF

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List of Comments		
#	Docket File	Submitter
66	EPA-HQ-OPPT-2019-0500-0066	Raymond Runyan, Professor of Cellular and Molecular Medicine, University of Arizona
67	EPA-HQ-OPPT-2019-0500-0067	Tony Tweedale, R.I.S.K. Consultancy
68	EPA-HQ-OPPT-2019-0500-0068	ToxStrategies for the ACC
69	EPA-HQ-OPPT-2019-0500-0069	Richard A. Denison, Lead Senior Scientist, EDF
70	EPA-HQ-OPPT-2019-0500-0070	Richard A. Denison, Lead Senior Scientist, EDF
71	EPA-HQ-OPPT-2019-0500-0071	Richard A. Denison, Lead Senior Scientist, EDF
72	EPA-HQ-OPPT-2019-0500-0072	J. M. DeSesso, and A. L. Williams
73	EPA-HQ-OPPT-2019-0500-0073	Jennifer McPartland, EDF
74	EPA-HQ-OPPT-2019-0500-0074	Jennifer McPartland, Richard Denison, and Lindsay McCorm, EDF
75	EPA-HQ-OPPT-2019-0500-0075	John M. DeSesso and Amy Lavin Williams, Exponent, Inc.
76	EPA-HQ-OPPT-2019-0500-0076	John M. DeSesso and Amy Lavin Williams, Exponent, Inc.
77	EPA-HQ-OPPT-2019-0500-0077	Nicholas Chartres, Research Scientist, Program on Reproductive Health and the Environment, University of California, San Francisco
78	EPA-HQ-OPPT-2019-0500-0078	Andre Ourso, Administrator, Center for Health Protection, Public Health Division, Oregon Health Authority (OHA) and Ali Mirzakkhalili, Air Division Administrator, State of Oregon Department of Environmental Quality (DEQ)
79	EPA-HQ-OPPT-2019-0500-0079	Stephen P. Risotto, Senior Director, ACC
80	EPA-HQ-OPPT-2019-0500-0080	Eric Berg, Deputy Chief, Research and Standards, California Division of Occupational Safety and Health (Cal/OSHA)
81	EPA-HQ-OPPT-2019-0500-0081	Elemar Marine Services Company
82	EPA-HQ-OPPT-2019-0500-0082	Lucas Allen, American Academy of Pediatrics et al.
83	EPA-HQ-OPPT-2019-0500-0083	Anonymous
84	EPA-HQ-OPPT-2019-0500-0084	Laura Reinhard, Vice President and General Manager, Honeywell International Inc.
85	EPA-HQ-OPPT-2019-0500-0085	Mass Comment Campaign sponsored by If It Was Your Child (web)
86	EPA-HQ-OPPT-2019-0500-0086	Mass Comment Campaign sponsored by If It Was Your Child (web)
87	EPA-HQ-OPPT-2019-0500-0087	Kari Rhinehart & Stacie Davidson, Co-Founders, If It Was Your Child
88	EPA-HQ-OPPT-2019-0500-0088	Mass Comment Campaign sponsored by EDF (17,321 signatories)
89	EPA-HQ-OPPT-2019-0500-0089	Anonymous

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List of Comments		
#	Docket File	Submitter
90	EPA-HQ-OPPT-2019-0500-0090	Trevor M. Penning, Director, Center of Excellence in Environmental Toxicology (CEET), University of Pennsylvania
91	EPA-HQ-OPPT-2019-0500-0091	Anonymous
92	EPA-HQ-OPPT-2019-0500-0092	Anonymous
93	EPA-HQ-OPPT-2019-0500-0093	Victoria Bogdan Tejeda, Associate Attorney, Earthjustice and Maria Lopez-Nuñez, Deputy Director, Organizing and Advocacy, Ironbound Community Corporation (ICC)
94	EPA-HQ-OPPT-2019-0500-0094	Christopher Bevan, Director, Scientific Programs, HSIA
95	EPA-HQ-OPPT-2019-0500-0095	Stephen P. Risotto, Senior Director, ACC
96	EPA-HQ-OPPT-2019-0500-0096	Rebecca J. Rentz, Senior Environmental Counsel, Occidental Chemical Corporation
97	EPA-HQ-OPPT-2019-0500-0097	Rebecca J. Bernstein, Senior Director, Product Safety & Regulatory Affairs, Health Environment & Safety, Arkema Inc.
98	EPA-HQ-OPPT-2019-0500-0098	Amy Chyao, Assistant Corporation Counsel and Amy McCamphill, Senior Counsel, Environmental Division, New York City Law Department
99	EPA-HQ-OPPT-2019-0500-0099	Liz Hitchcock, Director, SCHF et al.
100	EPA-HQ-OPPT-2019-0500-0100	Jonathan Kalmuss-Katz, Staff Attorney, Earthjustice and Randy Rabinowitz, Executive Director, Occupational Safety & Health Law Project
101	EPA-HQ-OPPT-2019-0500-0101	Richard Krock, Senior Vice President, Regulatory and Technical Affairs, Vinyl Institute (VI)
102	EPA-HQ-OPPT-2019-0500-0102	Julia M. Rege, Vice President, Energy & Environment, Alliance for Automotive Innovation
103	EPA-HQ-OPPT-2019-0500-0103	Suzanne Hartigan, Senior Director, Regulatory and Technical Affairs, ACC
104	EPA-HQ-OPPT-2019-0500-0104	Dianne C. Barton, Chair, National Tribal Toxics Council (NTTC)
105	EPA-HQ-OPPT-2019-0500-0105	Lauren Zeise, Director, Office of Environmental Health Hazard Assessment (OEHHA), California Environmental Protection Agency
106	EPA-HQ-OPPT-2019-0500-0106	Swati Rayasam et al., Science Associate, Program on Reproductive Health and the Environment, Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco (UCSF PRHE)
107	EPA-HQ-OPPT-2019-0500-0107	Diane VanDe Hei, Chief Executive Officer, Association of Metropolitan Water Agencies (AMWA)
108	EPA-HQ-OPPT-2019-0500-0108	EDF

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List of Comments		
#	Docket File	Submitter
109	EPA-HQ-OPPT-2019-0500-0109	Christopher Bevan, Director, Scientific Programs, HSIA
SACC	N/A	Science Advisory Committee on Chemicals (SACC)

1. Environmental Fate and Exposure

Environmental Fate and Exposure		
Charge Question 1.1: Please comment on EPA's qualitative analysis of pathways based on physical/chemical and fate properties (Section 2.1). **Charge Question 1.2:** Please comment on the data, approaches, and/or methods used to characterize exposure to aquatic receptors (Section 2.2). **Charge Question 1.3:** Please comment on EPA's assumption that TCE concentrations in sediment pore water are expected to be similar to the concentrations in the overlying water or lower in the deeper part of sediment, in which anaerobic conditions prevail. Thus, the TCE detected in sediments is likely from the pore (Section 4.1.3).		
#	**Summary of Comments for Specific Issues Related to Charge Question 1**	**EPA/OPPT Response**
Ecological populations assessed are incomplete		
SACC	**SACC COMMENTS:** Recommendation: Include additional discussion and justification for the decision to not assess risk to sediment and terrestrial organisms. The Committee questioned EPA's decision not to evaluate risk to sediment and terrestrial organisms based on low sorption and rapid volatilization even though TCE is one of the most widespread groundwater and soil gas contaminants in the United States.	For sediment-dwelling organisms, during problem formulation, EPA determined that an insignificant portion of TCE is available to enter the sediment compartment. Therefore, while the sediment pathway was included, EPA did not plan to further analyze exposure to sediment-dwelling species, and in the draft risk evaluation, sediment-dwelling organisms were only assessed qualitatively. However, in response to SACC comments a quantitative assessment of sediment-dwelling organisms was added to the final TCE risk evaluation in Section 4.1.3. For terrestrial organisms, during problem formulation exposure pathways to these organisms through water and biosolids were within scope, but not further analyzed, because physical-chemical properties do not support these pathways. The land-applied biosolids pathway is within the scope of the risk evaluation, but during

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		problem formulation EPA determined risks would not be quantitatively evaluated for land-applied biosolids because based on fate properties, TCE is not anticipated to partition to biosolids during wastewater treatment. Any TCE present in the water portion of biosolids following wastewater treatment and land application would be expected to rapidly volatilize into air. And the air exposure pathway from biosolids and surface water are insignificant. Based on the Guidance for Ecological Soil Screening Levels (EPA, 2003a, b) document, for terrestrial wildlife, relative exposures associated with inhalation and dermal exposure pathways are insignificant, even for volatile substances, compared to direct ingestion and ingestion of food (by approximately 1,000-fold). In addition, TCE is not expected to bioaccumulate in tissues, and concentrations will not increase from prey to predator in either aquatic or terrestrial food webs. EPA has added language to the final risk evaluation document in Section 4.1.4 explaining this rationale. For terrestrial organisms, pathways that were out of scope include ambient air from industrial sources, disposal in landfills, incineration units, and underground injection. Environmental exposure pathways covered under the jurisdiction of other EPA-administered statutes and regulatory programs are not within the scope of the risk evaluation. Emissions to ambient air from commercial and industrial stationary sources, and

		associated inhalation exposures of terrestrial species, are covered under the jurisdiction of the Clean Air Act (CAA). Pathways from disposal to sediment, soil, water, and air are covered under Resource Conservation and Recovery Act (RCRA), the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), CAA's Maximum Achievable Control Technology (MACT), and the Safe Drinking Water Act (SDWA). Clarifying language about what pathways are addressed under other statutes has been added to Section 1.4.2 of the Risk Evaluation.
SACC	**SACC COMMENTS:** Recommendation: Better justify exclusion in the exposure assessment of soil invertebrates and burrowing mammals in functionally confined spaces. In Section 3.1.5, volatilization rates are assumed to not contribute to exposure for terrestrial organisms. Several Committee members expressed concern regarding exposures to soil invertebrates and burrowing mammals in functionally confined spaces exposed to TCE through vapor intrusion from contaminated underground sources. This is considered in other Agency regulations (Comprehensive Environmental Response, Compensation, and Liability Act [CERCLA]) for human health concerns. A more robust justification or assessment is needed to dismiss exposures for these organisms. Another acceptable response may include appropriate jurisdiction by other laws or regulation. The Committee noted that acute exposures to terrestrial organisms that may spend significant time at the soil/air or water/air interface where volatilization may produce inhalation exposures cannot be ruled out.	As explained in more detail in Section 1.4.2 of the Final Risk Evaluation, EPA believes it is both reasonable and prudent to tailor TSCA Risk Evaluations when other EPA offices have expertise and experience to address specific environmental media, rather than attempt to evaluate and regulate potential exposures and risks from those media under TSCA. Section 1.4.2 has been updated to reflect the regulatory authority and risks addressed by CERCLA. For terrestrial organisms, during problem formulation exposure pathways to these organisms through water and biosolids were within scope, but not further analyzed, because physical-chemical properties do not support these pathways. The air exposure pathway from biosolids and surface water are insignificant. Based on the Guidance for Ecological Soil
56, 108	**PUBLIC COMMENTS:**	

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	EPA did not perform a quantitative assessment of exposures to terrestrial organisms because "TCE is not expected to partition to soil but is expected to volatilize to air, based on its physical-chemical properties." This statement ignores TCE exposures to terrestrial organisms through air, which is a primary pathway of exposure to TCE. EPA does not present or analyze data confirming this analysis. EPA dismisses exposure to terrestrial organisms from the ambient air pathway based on the unsupported argument that such exposures are adequately managed by the CAA. • TCE present in soil vapor will not degrade via atmospheric reactions. EPA has disregarded impacts from such exposure to terrestrial organisms whose habitat exists in the vadose zone. Fossorial and semi-fossorial organisms (those that burrow) have an "increased exposure potential from inhalation at site contaminated with volatile chemicals in the subsurface." EPA has ignored these sources of environmental exposure to such organisms. • Emission pathways to ambient air from commercial and industrial stationary sources or associated inhalation exposure of terrestrial species were considered to be outside of the scope of the risk evaluation because stationary source releases of TCE to ambient air are adequately assessed and any risks effectively managed when under the jurisdiction of the CAA.	Screening Levels (EPA, 2003a, b) document, for terrestrial wildlife, including soil invertebrates and burrowing mammals, relative exposures associated with inhalation and dermal exposure pathways are insignificant, even for volatile substances, compared to direct ingestion and ingestion of food (by approximately 1,000-fold). TCE is not expected to bioaccumulate in tissues, and concentrations will not increase from prey to predator in either aquatic or terrestrial food webs. In addition, concentrations will not increase from prey to predator in either aquatic or terrestrial food webs. EPA has added language to the final risk evaluation document in Section 4.1.4 explaining this rationale.
56, 108	**PUBLIC COMMENTS:** EPA is ignoring exposures to terrestrial organisms that may occur from contaminated water and soil. EPA must comprehensively consider all routes of exposure to terrestrial organisms in its risk evaluation. In addition to the fact that nearly two million pounds of TCE are released annually into the air, due to its volatility, disposal to water and land may also create a route of exposure to organisms living at the water-atmosphere or water-soil interface (*e.g.,* amphibians, birds and shorebirds, and burrowing organisms). • EPA has not provided rational and clear analysis based on the best available science and information to support its conclusions.	For terrestrial organisms, during problem formulation exposure pathways to these organisms through water and biosolids were within scope but not further analyzed, because physical-chemical properties do not support these pathways. The land-applied biosolids pathway is within the scope of the risk evaluation, but during problem formulation EPA determined risks would not be quantitatively evaluated for land-applied biosolids because based on fate

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		properties, TCE is not anticipated to partition to biosolids during wastewater treatment. Any TCE present in the water portion of biosolids following wastewater treatment and land application would be expected to rapidly volatilize into air. And the air exposure pathway from biosolids and surface water are insignificant. Based on the Guidance for Ecological Soil Screening Levels (EPA, 2003a, b) document, for terrestrial wildlife, relative exposures associated with inhalation and dermal exposure pathways are insignificant, even for volatile substances, compared to direct ingestion and ingestion of food (by approximately 1,000-fold). In addition, TCE is not expected to bioaccumulate in tissues, and concentrations will not increase from prey to predator in either aquatic or terrestrial food webs. EPA has added language to the final risk evaluation document in Section 4.1.4 explaining this rationale. For terrestrial organisms, pathways that were out of scope include ambient air from industrial sources, disposal in landfills, incineration units, and underground injection. Environmental exposure pathways covered under the jurisdiction of other EPA-administered statutes and regulatory programs are not within the scope of the risk evaluation. Emissions to ambient air from commercial and industrial stationary sources, and associated inhalation exposures of terrestrial species, are covered under the jurisdiction of the Clean Air Act (CAA). Pathways from disposal to

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		sediment, soil, water, and air are covered under Resource Conservation and Recovery Act (RCRA), the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), CAA's Maximum Achievable Control Technology (MACT), and the Safe Drinking Water Act (SDWA). Clarifying language about what pathways are addressed under other statutes has been added to Section 1.4.2 of the Risk Evaluation.
56, 108	**PUBLIC COMMENTS:** Impacts on sediment dwelling organisms need to be evaluated. • EPA stated in its problem formulation: "No data on the toxicity to sediment organisms were found; however, TCE is not expected to partition to sediment, based on physical chemical properties." Absence of hazard data does not equate to absence of hazard. A cursory review of the literature identified a study that found sensitivity of nematodes (sediment-dwelling organisms) to TCE at concentrations of 1 ug/ml (or 1000 ppb). At 30 mg/L, the researchers reported a significant reduction in the nematode maturity index, described as an index of diversity based on trophic groupings in nematodes in riparian soil microcosms. TCE has been measured in the sediment at concentrations of up to 26,000 µg/kg (or 26,000 ppb). • The scope of the draft risk evaluation limited the COUs included to those with applicable OESs. EPA then appears to have illogically limited its evaluation of risks to environmental receptors to just these COUs. As a result, it is likely that some environmental receptors potentially impacted by TCE discharges have been ignored because those discharges are not associated with a specific COU chosen based on worker exposure potential. Ignoring TCE-impacted sediment data illustrates this point. • EPA disregarded data associated with contaminated sites from its	For sediment-dwelling organisms, during problem formulation, EPA determined that an insignificant portion of TCE is available to enter the sediment compartment. Therefore, while the sediment pathway was included, EPA did not plan to further analyze exposure to sediment-dwelling species, and in the draft risk evaluation, sediment-dwelling organisms were only assessed qualitatively. However, in response to SACC comments a quantitative assessment of sediment-dwelling organisms was added to the final TCE risk evaluation in Section 4.1.3. EPA has evaluated the known, intended, and reasonably foreseen COUs for TCE, unless a COU was specifically excluded, and has not limited COUs only to OESs. Rather, OESs are used to group occupational COUs for purposes of risk evaluation.

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	water monitoring data ("Data Filtering and Cleansing," p. 89) and excluded monitoring data potentially impacted by Superfund sites in its watershed analysis ("Geospatial Analysis Approach," p. 89). While EPA acknowledges that TCE has been measured in sediments, it immediately dismisses these data, asserting that this detection is likely for TCE present in pore water; on this basis, EPA does not address risk to sediment-dwelling organisms. • Even if TCE were only associated with pore water, sediment-dwelling organisms often live in or are in contact with the pore water of sediment systems. Given that some of these organisms exist in the interstitial spaces in sediment and sand, pore water can be a key route of exposure to these organisms. Therefore, EPA cannot ignore this exposure pathway for sediment-dwelling organisms.	
108	**PUBLIC COMMENTS:** EPA ignores certain hazards by completely failing to provide quantitative analysis of environmental hazards to sediment-dwelling, terrestrial, or avian organisms (limiting such analysis to aquatic hazards). • EPA must analyze all of the environmental risks presented by TCE through ambient water. EPA did not analyze the risks to terrestrial or sediment-dwelling species from exposure through ambient water for TCE, despite the fact that terrestrial and sediment-dwelling species also can experience exposures through surface water. (p. 29). When EPA evaluates the risks presented by exposure through ambient water, EPA must consider the risks presented to terrestrial and sediment-dwelling ecological receptors as well as aquatic species.	For sediment-dwelling organisms, during problem formulation, EPA determined that an insignificant portion of TCE is available to enter the sediment compartment. Therefore, while the sediment pathway was included, EPA did not plan to further analyze exposure to sediment-dwelling species, and in the draft risk evaluation, sediment-dwelling organisms were only assessed qualitatively. However, in response to SACC comments a quantitative assessment of sediment-dwelling organisms was added to the final TCE risk evaluation in Section 4.1.3. For terrestrial organisms, during problem formulation exposure pathways to these organisms through water and biosolids were within scope, but not further analyzed, because physical-chemical properties do not support these pathways. The land-applied biosolids pathway is

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		within the scope of the risk evaluation, but during problem formulation EPA determined risks would not be quantitatively evaluated for land-applied biosolids because based on fate properties, TCE is not anticipated to partition to biosolids during wastewater treatment. Any TCE present in the water portion of biosolids following wastewater treatment and land application would be expected to rapidly volatilize into air. And the air exposure pathway from biosolids and surface water are insignificant. Based on the Guidance for Ecological Soil Screening Levels (EPA, 2003a, b) document, for terrestrial wildlife, relative exposures associated with inhalation and dermal exposure pathways are insignificant, even for volatile substances, compared to direct ingestion and ingestion of food (by approximately 1,000-fold). In addition, TCE is not expected to bioaccumulate in tissues, and concentrations will not increase from prey to predator in either aquatic or terrestrial food webs. EPA has added language to the final risk evaluation document in Section 4.1.4 explaining this rationale. For terrestrial organisms, pathways that were out of scope include ambient air from industrial sources, disposal in landfills, incineration units, and underground injection. Environmental exposure pathways covered under the jurisdiction of other EPA-administered statutes and regulatory programs are not within the scope of the risk evaluation. Emissions to ambient air from

		commercial and industrial stationary sources, and associated inhalation exposures of terrestrial species, are covered under the jurisdiction of the Clean Air Act (CAA). Pathways from disposal to sediment, soil, water, and air are covered under Resource Conservation and Recovery Act (RCRA), the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), CAA's Maximum Achievable Control Technology (MACT), and the Safe Drinking Water Act (SDWA). Clarifying language about what pathways are addressed under other statutes has been added to Section 1.4.2 of the Risk Evaluation.
Eco exposure concentration data/modeling/values are incomplete or invalid		
SACC	**SACC COMMENTS:** U.S. Environmental Protection Agency (EPA) expects limited exposure to aquatic organisms due to a high volatilization rate. However, trichloroethylene (TCE) only slowly biodegrades under aerobic conditions and the predicted volatilization half-lives in river waters (1.2 hours) and lake waters (110 hours) are not negligible.	Risk analysis for aquatic organisms is based on modeled surface water concentrations from E-FAST (U.S. EPA, 2014c) and monitored surface water concentrations.
SACC	**SACC COMMENTS:** Recommendation: Clarify why the Exposure and Fate Assessment Screening Tool (E-FAST), considered inappropriate for volatile organic compounds (VOCs), is relied on for evaluating environmental exposures. Committee members questioned why a comparison is performed between E-FAST modeled and measured data when, according to EPA documentation, the model is not appropriate for TCE, and stream flow data are not current. The Committee was uncertain on which data should be used to assess environmental exposures, since modeled data seemed inappropriate for the task and monitoring data are limited. A	EPA has conducted additional fate analysis for two sites with chronic COC (920 µg/L) exceedances (See Section 4.3.1 and 2.2.6.3). EPISuite fugacity modeling using WVOLWIN was conducted to inform the degree to which volatilization may impact the modeled stream concentrations estimated in E-FAST (U.S. EPA, 2014c). Parameters (wind speed, current speed, and water depth) reflective of two releasing sites with the highest predicted surface water concentrations (Praxair Technology Center in

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	Committee member questioned whether it is even appropriate to make the comparison between the two datasets. • One Committee member noted that the PDM portion of the E-FAST 2014 model was specifically written to handle surface runoff from nonpoint sources. It is used in this draft risk evaluation for determining the number of days exceeding the concentration of concern (COC) in free-flowing water bodies from a point source. The use of this model for evaluating a source with continuous point source releases needs justification because inputs to the model represent nonpoint source releases, not necessarily appropriate for point source releases. The draft risk evaluation has explicitly omitted non-point source releases. In using this model, it is unclear what assumptions are being made related to the upstream and initial downstream concentrations. Without further clarification, it is not possible for the Committee to comment on the appropriateness of this model in this evaluation. • A Committee member questioned whether the search for Superfund sites used five river miles or a simple five-mile radius from the water sampling point. If a Superfund site was within five miles, would Superfund site information be queried to determine that TCE exceeded a COC?	Tonawanda, NY and NASA Michoud in New Orleans, LA; see Table 4-1) were used to estimate TCE volatilization half-lives, which varied from one day to more than 10 years. The effect of volatility on estimating instream concentrations is expected to be highly variable and site-specific depending on stream flow and environmental conditions. For discharges to still, shallow water bodies, E-FAST estimates are less likely to overestimate surface water concentrations, as TCE is predicted to have a long half-life in such still water bodies. For discharges to faster-flowing, deeper water bodies, E-FAST estimates may inadequately reflect instream volatile losses expected within the timeframe of one day. Given this variation and the predicted half-life of TCE in flowing water bodies, E-FAST surface water concentrations may best represent concentrations found at the point of discharge. EPA agrees that the lack of colocation between monitored values of TCE and estimated surface water concentrations from known releases for the majority of results makes it difficult to draw definitive conclusions. Nevertheless, the evaluated monitoring data within the United States from recent years showed that the majority of samples had detectable levels of TCE below identified COCs. EPA appreciates the suggestion to do modeling across similar classes of chemicals to evaluate model performance and predictive ability and will consider those

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		suggestions for future risk evaluations. However, absent monitoring programs designed to measure these concentrations proximal to discharging facilities, the colocation of monitoring information with known facility releases is expected to be small thereby limiting model verification with actual monitored values. The scope of this EPA TSCA risk evaluation does not include on-site releases to the environment of trichloroethylene at Superfund sites and subsequent exposure of the general population or non-human species. However, the geospatial analysis component of the aquatic exposure assessment included a search for Superfund sites within 1 to 5 miles of the surface water monitoring stations. Superfund sites in 2016 were identified and mapped using geographic coordinates of the "front door," as reported in in Envirofacts; therefore, EPA did not utilize the five river miles noted by the commenter. Co-location of releasing facilities and monitoring sampling locations was examined for presence in the same watershed (HUC-8 and HUC-12). Co-location does not necessarily indicate there is an upstream/downstream connection between release and sampling sites. The monitoring stations co-located with facilities in the same HUC in the 2016 dataset were also examined for proximity to Superfund sites; however, no Superfund sites were identified within five miles of these sites.
56, 108	**PUBLIC COMMENTS:**	

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	The EPA based its exposure estimates on unreliable surface water concentrations and uncertain calculations. EPA ignored environmental impacts to surface water from TCE discharges, and the existing surface water data may not be representative of TCE concentrations. EPA acknowledges the limitations of data in the U.S. Geological Survey (USGS)-National Water Information System (NWIS) and STOrage and RETrieval (STORET) databases. • When calculating surface water release estimates, EPA correctly states that "release estimates serve as the key inputs into the exposure mode and are therefore a key component of the overall aquatic exposure scenario confidence." Based on available data, and other considerations relating to the estimation of rates of discharges from various facilities – including outdated stream flow data in E-FAST, some of which are decades old – EPA was over-generous in assigning a "moderate" confidence in wastewater discharge estimates. EPA applied a wastewater treatment removal rate of 81% to all indirect releases, as well as to direct releases from wastewater treatment plants (WWTPs). EPA did not establish that this assumed that removal actually occurs, so EPA may be underestimating the total risk presented by releases from these facilities.	EPA utilized national surface water monitoring datasets from the WQP/WQX, as well as published literature obtained and evaluated for quality through a systematic review process. Uncertainties underlying the modeling approach are discussed in Section 2.2.6.3. EPA has corrected the footnotes to state that the 81% removal rate was applied to indirect releases only. The supplemental file [Aquatic Exposure Modeling Outputs from E-FAST] demonstrates than 0% removal is applied to numerous WWTP or POTW facilities, if they were categorized as direct releasers. The WWR% of 81% was applied, when appropriate, to volumes characterized as being transferred off-site for treatment at a water treatment facility prior to discharge to surface water. A WWR% of zero was used for direct releases to surface water because the release estimates are based on estimated release (post-treatment).
Physical-chemical properties are not valid or complete		
56, 108	**PUBLIC COMMENTS:** EPA reported that the organic carbon:water partition coefficient (log K_{oc}) for TCE ranged between 1.8 and 2.17, which generally suggests that soil and sediment sorption of TCE is low. Other EPA sources cite a moderately higher log K_{oc} of 2.4, and note that in practice, "[m]easured partition coefficients, however, may be considerably higher than calculated values, especially at lower aqueous concentrations." TCE partitioning in the environment is affected by more than just organic carbon, and there are numerous sorption studies for TCE. One such study, conducted at the Savannah River Site, noted that measured soil	Although the log K_{OC} indicates that TCE will partition to sediment organic carbon, organic matter typically comprises 25% or less of sediment composition (*e.g.,* https://pubs.usgs.gov/of/2006/1053/downloads/pdf/of-2006-1053.pdf) of which approximately 40-60% is organic carbon (Schwarzenbach et al., 2003). Based on these values, the sediment-water K_d (where $K_d = K_{OC} * f_{OC}$) is expected to be

	distribution coefficient values for TCE were "60 to 100 times higher than those estimated based on [sediment organic fraction] and KOC." The predicted value that EPA relies on for TCE associated with soil could well underestimate what is actually present.	equal to or less than 9.5, indicating that at equilibrium, concentrations in sediment would be expected to be less than 10 times higher than in porewater. For a log K_{OC} of 2.4 concentrations in sediment would be expected to be less than 38 times higher than in porewater. In either case TCE is expected to be in sediment and pore water with concentrations similar to or less than the overlying water due to partitioning to organic matter in sediment and biodegradability in anaerobic environments. Ecotoxicity from ingestion of sediments was not quantitatively evaluated. Discussion of the partitioning of TCE between sediment solids and pore water has been added to Section 2.1.2 Summary of Fate and Transport. In the case of spills or leaks of TCE, TCE may sink in water and fill sediment pore space as a dense non-aqueous phase liquid (DNAPL), resulting in sediment concentrations many times higher than would be predicted by partitioning to sediment by TCE dissolved in water. However, such spills and leaks from legacy disposal, as at SRS, are not considered to be within the scope of the risk evaluation.
SACC	**SACC COMMENTS:** Recommendation: Explain why estimated K_{oc} values are used in place of measured values. There are many experimentally derived estimates of TCE's sorption coefficient that are available in the literature that show values ranging as high as a log K_{oc} of 4.2 (*e.g.,* see Allen-King et al., 1997). Committee	EPA's literature search for environmental fate properties did not identify any studies measuring K_{OC} thus systematic review was not performed for the endpoint. There are two K_{OC}-estimation methods included in the EPI Suite™ KOCWIN

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	members questioned why a predicted value of log K_{oc} is used when there are experimentally derived values available.	module. The value produced by the molecular connectivity index (MCI) method was presented in the draft risk evaluation and is somewhat less than the value estimated using the regression from log K_{OW} (log K_{OC} = 2.1 by log K_{OW} and 1.8 by MCI). Table 2-1 has been edited to present both estimated log K_{OC} values.
SACC	**SACC COMMENTS:** Recommendation: Include the range of physical-chemical properties where multiple values are available. It is not clear how the physical-chemical properties listed in Table 1-1 were selected over other values reported in the literature (many of which are listed in the supplemental data) or why a range of values is not provided. A range of physical-chemical properties should be reported and used in the environmental fate modeling to determine how sensitive the models are to the key chemical input properties.	Although the physical and chemical properties selected for use in the TCE risk evaluation were primarily drawn from the PhysProp database in EPI Suite™ (U.S. EPA, 2012b), those data were selected from among the values collected from the publicly-accessible Reaxys, ChemSpider, STN/CAS, and PhysProp (integrated into EPI Suite™) databases and from data submitted to EPA under the authority of various TSCA sections. EPA used p-chem properties data from studies with the highest Systematic Review data quality evaluation scores for use in the Risk Evaluation.
56, 108	**PUBLIC COMMENTS:** The physical-chemical properties of TCE will lead to longer half-lives in water than predicted by the Estimation Programs Interface Suite (EPI Suite™) volatilization module, which likely biases predictions of concentrations in surface water to be artificially low. In its draft risk evaluation, EPA reports the modeled volatilization half-life of TCE in a model river will be 1.2 hours and the half-life in a model lake will be 110 hours. TCE is a dense non-aqueous phase liquid (DNAPL). In its 2014 TCE work plan risk assessment, EPA notes that TCE's "density may cause it to sink in the water column, potentially increasing the aquatic residence time of TCE." It further notes that the "[v]olatilization	A discussion of the uncertainty in the estimation of TCE volatilization half-lives from water has been added to section 2.1.3, Assumptions and Key Sources of Uncertainty for Fate and Transport in the final Risk Evaluation. Under the conditions of use for TCE examined under this final Risk Evaluation, it is not expected that TCE would be found at concentrations greater than 1% of its aqueous solubility, or 12,800 ug/L. Under conditions in which TCE is present in surface

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	half-lives in an experimental field mesocosm consisting of seawater, planktonic, and microbial communities ranged from 10.7 to 28 days," contrasting those values to measured "half-lives of evaporation from laboratory water surfaces (distilled water) [that] have been reported to be on the order of several minutes to hours, depending upon the turbulence." This suggests that the volatilization half-life used by EPA in this evaluation is too low. Even considering less-turbulent water bodies (lakes), the half-life reported by EPA is one-half to one-fifth the value of that found in natural conditions. • The density of TCE, coupled with its relatively low solubility, indicates that sampling surface water using grab samples at the tops of water columns will bias the analysis, resulting in artificially low environmental concentrations. Such an approach to sampling may not represent the actual concentrations of TCE found in surface water.	water at concentrations of less than 1% of its solubility, the physical and chemical properties of TCE that lead to TCE's classification as a DNAPL are not likely to increase the residence time in surface water. Mesocosm tests do not necessarily simulate the turbulence in natural systems, and it would therefore be expected that decreased rates of volatilization would be observed under mesocosm conditions where the effects of wind velocity, water velocity, turbulence, and mixing are not representative of environmental conditions.
Fate assumptions/models are not valid or complete		
SACC	**SACC COMMENTS:** Recommendation: Modify the discussion on the lack of TCE in biosolids based on the suitability of the analytical methods used in the cited surveys. The draft risk evaluation states that TCE is not anticipated to partition to biosolids during wastewater treatment, reporting that TCE is not detected in the Targeted National Sewage Sludge Survey (TNSSS) nor is it reported in biosolids during EPA's Biennial Reviews for Biosolids, a robust biennial literature review conducted by EPA's Office of Water (U.S. EPA, 2019). The Committee noted that the methods used to analyze the biosolids in these surveys are not suitable for TCE and that the targeted analysis did not appear to specifically look for TCE.	During problem formulation EPA determined risks would not be evaluated for land-applied biosolids because based on fate properties, TCE is not anticipated to partition to biosolids during wastewater treatment. Any TCE present in the water portion of biosolids following wastewater treatment and land application would be expected to rapidly volatilize into air. In addition, TCE is not expected to bioaccumulate in tissues, and concentrations will not increase from prey to predator in either aquatic or terrestrial food webs. Lastly, based on the Guidance for Ecological Soil Screening Levels (EPA, 2003a, b) document, for terrestrial wildlife, relative exposures associated with
47	**PUBLIC COMMENTS:** Modeling based on physical and chemical properties and fate parameters support the view that TCE is not expected to partition to biosolids and sediment in sewage treatment plants. There is agreement	

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	with EPA's draft risk evaluation to conduct no further analysis beyond what was done in the problem formulation document for environmental exposure pathways for land application of biosolids and sediment and water or soil pathways for terrestrial organisms. Physical and chemical properties confidently predict TCE will be mobile in soil and migrate to water, or volatilize to air.	inhalation and dermal exposure pathways are insignificant, even for volatile substances, compared to direct ingestion and ingestion of food (by approximately 1,000-fold). EPA has added language to the final risk evaluation document in Section 4.1.4 explaining this rationale.
103	**PUBLIC COMMENTS:** EPA should explain its approach to the assessment of the environmental fate of TCE clarify the assumptions and limitations associated with fugacity modeling. EPA's approach includes some measured data, as well as estimates from EPI Suite™. Fugacity models require detailed understanding of the inputs in order to appropriately interpret the model outputs. This is particularly challenging for the EPI Suite™ model due to the setup of the interface. • Fugacity modeling should be conducted as a tiered process. Multimedia models are available via the Chemical Properties Research Group website, including Level I and Level II models, that can provide access to the various inputs. EPA should provide more detail regarding the inputs for fugacity modeling and explain limitations associated with this information for the purposes of risk assessment. • EPA should address the Science Advisory Committee on Chemicals (SACC) comments that the Level III fugacity model seemed to indicate that TCE emissions to the air could ultimately result in higher concentrations in the water. However, there are a number of assumptions and limitations to the model. EPA should clarify these assumptions and limitations in its final risk evaluation of TCE to more fully explain why EPA's approach was appropriate.	Discussion of fugacity modeling has been added to Section 2.1 Fate and Transport.
56, 108	**PUBLIC COMMENTS:** Partition coefficients assume that chemical equilibrium has been established. However, chemicals of concern can occur in high concentrations in different environmental compartments prior to	During problem formulation EPA conducted a screening level analysis to consider whether pathways of exposure for sediment and terrestrial

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	reaching equilibrium. When considering an open, multi-media system, a better approach for approximation might be the Level III Fugacity model, which predicts that 9.9% of TCE will be distributed to soil, 36.8% to air, 53% to water, and the remainder (0.26%) to sediment, as calculated using EPI Suite 4.11. A 10% percent distribution to soil cannot be dismissed as *de minimis*.	organisms should be further analyzed and determined that terrestrial organism exposures to TCE was not of concern partially based on estimates of soil concentrations from evaluated COUs being several orders of magnitude below concentrations observed to cause effects in terrestrial organisms. For sediment-dwelling organisms, during problem formulation, EPA determined that an insignificant portion of TCE is available to enter the sediment compartment. Therefore, while the sediment pathway was included, EPA did not plan to further analyze exposure to sediment-dwelling species, and in the draft risk evaluation, sediment-dwelling organisms were only assessed qualitatively. However, in response to SACC comments a quantitative assessment of sediment-dwelling organisms was added to the final TCE risk evaluation in Section 4.1.3.
SACC	**SACC COMMENTS:** Kinetics cannot be directly inferred from equilibrium properties. The rate of volatilization depends on environmental conditions more than equilibrium properties. K_{oc} values are assumed to reflect equilibrium. Sorption kinetics depend on the chemical and sorbent combination. When considering exposure pathways, it is important to note that movement between compartments goes both ways based on equilibrium. For instance, movement from water to air is only true in scenarios where air does not contain significant TCE concentrations.	Chemical kinetics are included in the Fugacity, STPWIN, and Water Volatilization models which use the two-film model to estimate the rate of transfer between air and water. The two-film model uses mass transfer coefficients with units of meters per hour to account for the rate at which chemicals move toward or away from the air-water interface. The equilibrium coefficient (*i.e.,* Henry's Law Constant) is only used to estimate the air or water concentration at the air-water interface where equilibrium conditions exist.

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56, 108	**PUBLIC COMMENTS:** The high volatility of TCE leads to air exposure through releases to soil and water, not just through direct emissions to ambient air. When TCE moves to the atmosphere, its half-life through degradation by reactants in the atmosphere is nearly two weeks, which has led EPA to conclude that "long range transport is possible." The logical conclusion is that land-applied TCE and TCE-contaminated wastewater sent to treatment facilities are likely an important source of air-exposures of TCE, which EPA has not addressed. • This type of degradation will only occur in the atmosphere. However, migration of TCE in soil does not always result in volatilization to the atmosphere. EPA notes that, "in soil, TCE can become associated with soil pore water, enter the gas phase…, or exist as a nonaqueous phase liquid (NAPL). It is possible that upward or downward movement of TCE can occur in each of these three phases."	For terrestrial organisms, during problem formulation exposure pathways to these organisms through water and biosolids were within scope, but not further analyzed, because physical-chemical properties do not support these pathways. The land-applied biosolids pathway is within the scope of the risk evaluation, but during problem formulation EPA determined risks would not be quantitatively evaluated for land-applied biosolids because based on fate properties, TCE is not anticipated to partition to biosolids during wastewater treatment. Any TCE present in the water portion of biosolids following wastewater treatment and land application would be expected to rapidly volatilize into air. And the air exposure pathway from biosolids and surface water are insignificant. Based on the Guidance for Ecological Soil Screening Levels (EPA, 2003a, b) document, for terrestrial wildlife, relative exposures associated with inhalation and dermal exposure pathways are insignificant, even for volatile substances, compared to direct ingestion and ingestion of food (by approximately 1,000-fold). In addition, TCE is not expected to bioaccumulate in tissues, and concentrations will not increase from prey to predator in either aquatic or terrestrial food webs. EPA has added language to the final risk evaluation document in Section 4.1.4 explaining this rationale. Additionally, based on its vapor density (2.93

		relative to air) and atmospheric oxidation half-life of 1 to 11 days (Table 2-1), TCE vapor may accumulate under specific conditions, but typically will disperse readily into the air. For these reasons, the final risk evaluation does not include further analysis of this pathway to terrestrial species, and EPA was able to assess risk based on qualitative analysis.
SACC	**SACC COMMENTS:** According to one Committee member, EPA discounts the findings of their own 2014 TCE Work Plan (p. 158, C-1-3). For example, the environmental fate sections in that document state: "there are several factors that can limit the aerobic biodegradation of TCE, including TCE concentration, pH, and temperature. Toxicity of the degradation products (*e.g.,* dichloroethylene, vinyl chloride, chloromethane) to the degrading microorganisms may also reduce the rates of biodegradation of TCE in aerobic soils."	The rate of aerobic biodegradation is the key area of uncertainty in the fate assessment for TCE. A description of this has been added to the fate section (2.1.3). Due to the differences among study conditions, generating confidence intervals for each property would be very complex. However, the range and quality of available data were considered in the fate assessment of TCE.
SACC	**SACC COMMENTS:** The Committee continued to be concerned about the potential impact of groundwater to surface water pathway to the evaluation. Members also mentioned that landfill releases to surface water should be included inasmuch as they derive from current uses of TCE. If the partitioning to sediments and soil is considered minimal, then the risk to groundwater, especially unregulated drinking water sources, must be objectively determined. Furthermore, TCE-contaminated storm water must have resulted from landfill and industrial use and should be assessed.	Landfill exposures were not included in the environmental exposure conceptual model or assessed because disposal of TCE via underground injection, RCRA Subtitle C hazardous waste landfills, RCRA Subtitle D municipal solid waste (MSW) landfills, and on-site releases to land from industrial non-hazardous waste and construction/demolition waste landfills are covered under the jurisdiction of RCRA. Because the drinking water exposure pathway for TCE is covered in the SDWA regulatory analytical process for public water systems, EPA

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		did not include this pathway in the risk evaluation for TCE under TSCA.
SACC	**SACC COMMENTS:** Recommendation: Include a diagram that displays pathway and rates (*e.g.,* biodegradation, exchange, discharge). • Members commented that the qualitative analysis is generally adequate, but some members found this draft risk evaluation for TCE less concise and more difficult to read than previous evaluations.	An environmental fate diagram for TCE has been inserted into section 2.1 Environmental Fate and Transport.
SACC	**SACC COMMENTS:** Recommendation: Include additional discussion on uncertainties for exposure based on the potential for persistent exposure. • Based on the log K_{ow} and predicted log K_{oc}, EPA predicts limited partitioning into biosolids. EPA states that this is confirmed with TNSSS data (reference not provided in the draft risk evaluation), which did not detect TCE. While a similar argument is made for partitioning into sediments, there are no measured data to support this qualitative estimate. • Additional text regarding uncertainties for the predictions is needed. For example, EPA indicates that TCE would not bioaccumulate based upon a log K_{ow} of ~2. This value indicates that TCE would partition into the organic phase 100 times more than in the aqueous phase. If TCE is continuously discharged into aquatic systems, "pseudo-persistent" exposure would occur because there is limited aerobic biodegradation. While only 1% is predicted to be discharged into surface water from EPI Suite™, based on the production volume and multiple detections observed in surface waters across the United States, persistent exposure may be a possibility and should be addressed as an uncertainty.	During problem formulation EPA determined risks would not be evaluated for land-applied biosolids because, based on fate properties, TCE is not anticipated to partition to biosolids during wastewater treatment. Any TCE present in the water portion of biosolids following wastewater treatment and land application would be expected to rapidly volatilize into air. And the air exposure pathway from biosolids and surface water are insignificant. Based on the Guidance for Ecological Soil Screening Levels (EPA, 2003a, b) document, for terrestrial wildlife, relative exposures associated with inhalation and dermal exposure pathways are insignificant, even for volatile substances, compared to direct ingestion and ingestion of food (by approximately 1,000-fold). In addition, TCE is not expected to bioaccumulate in tissues, and concentrations will not increase from prey to predator in either aquatic or terrestrial food webs. EPA has added language to the final risk evaluation document in Section 4.1.4 explaining this rationale.

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		For sediment-dwelling organisms, during problem formulation, EPA determined that a significant portion of TCE is available to enter the sediment compartment. Therefore, while the sediment pathway was included, EPA did not plan to further analyze exposure to sediment-dwelling species, and in the draft risk evaluation, sediment-dwelling organisms were only assessed qualitatively. However, in response to SACC comments, a quantitative assessment of sediment-dwelling organisms was added to the final TCE risk evaluation in Section 4.1.3.
SACC	**SACC COMMENTS:** Recommendation: Add confidence intervals to the estimate of proportional removal and conduct a model sensitivity analysis to determine if variability associated with the physical-chemical properties would change EPA's fate assessment. • The draft risk evaluation states that the Sewage Treatment Plant (STP) model in EPI Suite™ predicts 81% removal via volatilization and 1% removal via sorption. It is further stated that TCE is not reported in EPA's Biennial Review for Biosolids. The 81% removal is used in subsequent modeling efforts without considering any variability as is the 1% removal via sorption.	Due to the differences among study conditions, generating confidence intervals for each property would be very complex. However, the range and quality of reasonably available data were considered in the fate assessment of TCE. For the TCE Risk Evaluation the STP model in EPI Suite™ (U.S. EPA, 2012b) was run using the assumption that TCE would not biodegrade during aerobic treatment. Physical-chemical properties input from table 1-1 were used. A sensitivity analysis varying key physical-chemical properties driving removal of TCE by volatilization was also conducted. The results indicated that a 25 percent increase in the value of TCE vapor pressure, water solubility or Kow input to the STP model made no more than a one percent difference in removal of TCE by volatilization or adsorption to activated sludge. The 25 percent value was chosen to represent hypothetical variability around the values of the

		water solubility, vapor pressure and Kow input to the STP model. Because the STP model output changes very little when inputs vary around a 25% change in their values, a single removal estimate was considered adequate for the purpose of estimating removal in wastewater treatment.
SACC	**SACC COMMENTS:** If release is to lake waters (110-hour half-life), is daily averaging an appropriate measure of average water concentrations (there is an issue of carry-over of the undegraded fraction from day one added to new releases on day two)?	Some of the releasing facilities did discharge to still water bodies such as lakes or bays, for which surface water concentrations are estimated using a dilution factor rather than a stream flow distribution. However, the analysis did not estimate or aggregate undegraded TCE day over day. This has been added to the uncertainties discussion in Section 2.2.6.3.
SACC	**SACC COMMENTS:** There is no mention of the influence that TCE density has on environmental fate. TCE density and partitioning to suspended sediments means that TCE will deposit in bottom sediments, where it may form a DNAPL. Density-dependent deposition to sediments is acknowledged, but not considered in the draft risk evaluation.	EPA added discussion of uncertainty in considering the influence of TCE density on environmental fate in Section 2.1.3., Assumptions and Key Sources of Uncertainty for Fate and Transport.
SACC	**SACC COMMENTS:** Wipe cleaning – uses towels, rags, paper – may end up in landfills. What impact would there be, if any, from this slow release of TCE to the environment?	Landfill exposures were not included in the environmental exposure conceptual model or assessed because disposal of TCE via underground injection, RCRA Subtitle C hazardous waste landfills, RCRA Subtitle D municipal solid waste (MSW) landfills, and on-site releases to land from industrial non-hazardous waste and construction/demolition waste landfills are covered under the jurisdiction of RCRA.

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Mass balance approach recommended		
SACC	**SACC COMMENTS:** Recommendation: Provide better mass balance analysis to determine whether unaccounted TCE should be considered an environmental release. • Most of the Committee discussed the desire for a "mass balance" approach particularly for environmental exposure. • The problem formulation document (U.S. EPA, 2018) indicated that recycling and disposal at 172 reporting facilities totaled 91,000,000 pounds. Yet the draft risk evaluation assesses only 52 pounds of releases. It is scientifically indefensible to disregard 91,000,000 pounds of reported emissions from reporting facilities and base a nationwide environmental risk assessment on 0.003% of the known releases. Similarly, the Toxics Release Inventory (TRI) reported 91,000,000 pounds released is a fraction of the 172,000,000 pounds used in commerce. Much of the remainder is unaccounted for. • Some Committee members noted the difficulty of assigning any "unaccounted TCE" to a condition of use (COU). Other Committee members emphasized that 83.6% of TCE manufactured/imported is known to be consumed in the production of refrigerant 134a.	EPA's analysis uses TRI (U.S. EPA, 2017g) and DMR (U.S. EPA, 2016a) to estimate the highest local per site water releases of TCE. EPA has added a mass balance analysis as suggested to Appendix R of the Risk Evaluation. Based on use patterns for TCE, approximately 84% of manufactured and/or imported TCE is consumed during manufacturing refrigerants.
108	**PUBLIC COMMENTS:** • EPA's risk evaluation lacks an adequate mass balance. EPA's draft risk evaluations have failed to account for a chemical substance's presence and flow at the different stages of its lifecycle. In the case of TCE, over 170 million pounds of TCE are manufactured in or imported into the United States annually, yet only about 2.2 million pounds of TCE were identified as released to the air, water, and land; the draft risk evaluation does not make clear where the rest of it goes. According to the Emergency Planning and Community Right-to-Know act (EPCRA), mass balance is "an accumulation of the annual quantities of chemicals transported to a facility, produced at a facility, consumed at a facility, used at a facility, accumulated at a facility, released from a	

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	facility, and transported from a facility as a waste or as a commercial product or byproduct or component of a commercial product or byproduct." While EPA relies on the Chemical Data Reporting (CDR) and TRI to compile some estimates of these values, there are limitations on both of those reporting schemes that result in an incomplete picture of the chemical's lifecycle.	
TCE concentrations in sediment pore water are/are not valid		
47	**PUBLIC COMMENTS:** EPA did not quantitatively assess exposure to sediment-dwelling organisms because TCE is expected to remain in aqueous phases and not adsorb to sediment due to its water solubility and low partitioning to organic matter. Limited sediment monitoring data for TCE suggest that TCE is present in sediments, but because of its relatively low partition coefficient for organic matter and because it biodegrades slowly, TCE concentrations in sediment pore water are expected to be similar to the concentrations in the overlying water or lower in the deeper part of sediment where anaerobic conditions prevail. Thus, TCE detected in sediments is likely from the pore water. There is agreement with EPA's assessment and decision not to further pursue characterizing risks due to TCE exposure to sediment-dwelling organisms.	For sediment-dwelling organisms, during problem formulation, EPA determined that an insignificant portion of TCE is available to enter the sediment compartment. Therefore, while the sediment pathway was included, EPA did not plan to further analyze exposure to sediment-dwelling species, and in the draft risk evaluation, sediment-dwelling organisms were only assessed qualitatively. However, in response to SACC comments a quantitative assessment of sediment-dwelling organisms was added to the final TCE risk evaluation in Section 4.1.3.
SACC	**SACC COMMENTS:** The Committee noted that it appears likely that TCE pore-water concentrations are similar to overlying water. The movement from sediment is dependent upon the organic carbon content of the sediment. With a predicted log K_{oc} of ~2, the likelihood that TCE will be in organic carbon is 100 times greater. The lack of detected TCE in sewage sludge, which has high concentrations of organic carbon, suggests that partitioning into pore water does occur even with this log K_{oc}.	Although the log K_{oc} indicates that TCE will partition to sediment organic carbon, organic matter typically comprises 25% or less of sediment composition (*e.g.,* https://pubs.usgs.gov/of/2006/1053/downloads/pdf/of-2006-1053.pdf) of which approximately 40-60% is organic carbon (Schwarzenbach et al., 2003). Based on these values, the sediment-water Kd (where Kd = KOC*fOC) is expected to be equal to or less than 9.5, indicating that at equilibrium, concentrations in sediment would be expected to be less than ten times higher than in

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		porewater. However, the porewater interacts with overlying surface water from which TCE may be lost via volatilization. Thus, concentrations in sediment and pore water are expected to be equal to or less than concentrations in overlying water. A narrative to this effect has been added to the final risk evaluation (Section 2.1)
EPA should obtain/use measured data on TCE levels in sediments		
56, 108	**PUBLIC COMMENTS:** EPA has ignored STORET data available for evaluating sediment impacts. As a DNAPL, TCE is likely to be present in the sediment, at the bottom of a water column. In its problem formulation EPA noted that the STORET database would be examined for recent data on TCE levels in sediment. However, these data are absent from the draft risk evaluation. A review and analysis of data reported in the National Water Quality Monitoring Council database of Water Quality Data for TCE in sediment (above detection) in the last 10 years resulted in 21 quantifiable analyses of TCE in sediment; the maximum detected concentration was 26,000 µg/kg. • EPA overlooked these data, which are environmentally relevant and describe measured impacts to environmental systems, simply because of its assertion that TCE "is not expected to accumulate in sediments."	STORET data showing detections in 6% of samples was analyzed by (Staples et al., 1985), and summarized by ATSDR, which stated that the median concentration measured in sediment was < 5 µg/kg (dry weight), equivalent to 5 ppb, which is more than 2 orders of magnitude below the chronic (920 ppb) and acute concentration of concern (COC) (2,000 ppb) values estimated for sediment invertebrates by read-across from COCs reported for aquatic invertebrates. Although the log K_{oc} indicates that TCE will partition to sediment organic carbon, organic matter typically comprises 25% or less of sediment composition (*e.g.,* https://pubs.usgs.gov/of/2006/1053/downloads/pdf/of-2006-1053.pdf) of which approximately 40-60% is organic carbon (Schwarzenbach et al., 2003). Based on these values, and using a log K_{oc} of 1.8 the sediment-water K_d (where $K_d = K_{oc}*f_{oc}$) is expected to be equal to or less than 9.5, indicating that at equilibrium, concentrations

		in sediment would be expected to be less than ten times higher than in porewater. However, biodegradation can be expected to be rapid in anaerobic sediments and the porewater also interacts with overlying surface water from which TCE may be lost via volatilization and/or aerobic biodegradation. Thus, concentrations in sediment and pore water are expected to be equal to or less than concentrations in overlying water. A narrative to this effect has been added to the final risk evaluation (Section 2.1).
SACC	**SACC COMMENTS:** Recommendation: Consider obtaining measurements of TCE in sediments near release sites. • The draft risk evaluation does not consider the fact that a K_{oc} of between 60 and 126 demonstrates higher TCE concentrations in sediment than in water for all situations where sediment organic carbon (OC) is 0.8-1.6% of the water mass. Sediments most often have OC content much higher than 1.6%. These values are relatively simple to obtain from the USGS or from direct measurements in sediments near discharging facilities. • The draft risk evaluation seems to assume that all systems are at thermodynamic equilibrium and that kinetics do not exist. Water in sediment (*i.e.,* pore water) and overlying water can only be at equilibrium with high turbulence and at significant distance downriver from inflow. In sediments of rivers with low turbulence, only the first few centimeters of sediment are in equilibrium with overlying water. There is virtually no advection between stationary sediment and water. So, once TCE-laden sediments are deposited, the TCE is less likely to partition back into water than might be predicted in ideal situations. Measurements of TCE in sediments near commercial releases are needed. • A Committee member noted that the partition coefficient from	Although the log K_{oc} indicates that TCE will partition to sediment organic carbon, organic matter typically comprises 25% or less of sediment composition (*e.g.,* https://pubs.usgs.gov/of/2006/1053/downloads/pdf/of-2006-1053.pdf) of which approximately 40-60% is organic carbon (Schwarzenbach et al., 2003). Based on these values, the sediment-water Kd (where Kd = K_{oc} *f_{oc}) is expected to be equal to or less than 9.5, indicating that at equilibrium, concentrations in sediment would be expected to be less than 10 times higher than in porewater. A narrative to this effect has been added to the final risk evaluation, in a subsection of Section 2.1. STORET data showing detections in 6% of samples was analyzed by (Staples et al., 1985), and summarized by ATSDR, which stated that the median concentration measured in sediment was < 5 µg/kg (dry weight), equivalent to 5 ppb, which is more than 2 orders of magnitude below

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	measured data (U.S. EPA, 1977) shows field measured partition coefficients of 0.076 and 0.32 when using geometric mean and arithmetic mean concentrations in water and sediment media, respectively. The draft risk evaluation should justify that 0.32 (32%) represents low partitioning to sediments. • The review of available data raised questions regarding the extent to which TCE may be present in sediments, yet no monitoring studies have been conducted to refute the available data. This means that the draft risk evaluation erroneously states that "review and evaluation of reasonably available information on TCE confirmed" problem formulation conclusions.	the chronic (920 ppb) and acute concentration of concern (COC) (2,000 ppb) values estimated for sediment invertebrates by read-across from COCs reported for aquatic invertebrates.
Considerations of TCE either as a degradant/byproduct or degradants/byproducts of TCE		
SACC, 56, 108	**SACC COMMENTS:** Recommendation: Include available information on specific degradation/hydrolysis substances in the draft risk evaluation. • Several sections of the draft risk evaluation state that anaerobic biodegradation of TCE is rapid. The Committee noted that this is not always the case, and in many situations, toxic biodegradation intermediates are formed, including dichloroethylene and vinyl chloride. Atmospheric photolysis via the hydroxyl radical (OH) also can result in the formation of chloroform and other chlorinated byproducts (Itoh et al., 1994). **PUBLIC COMMENTS:** EPA concluded that the rate of anaerobic biodegradation is "fast." Under ideal conditions with correct microbial consortia that carry the metabolic capability to reductively dehalogenate TCE to ethene, this conclusion is valid; however, there are important caveats. EPA acknowledges that there is inherent variability in the reported biodegradation rates, yet still concludes that the "weight of evidence shows the anaerobic biodegradation in anaerobic condition is fast." • Biologically mediated processes that transform compounds cannot be assumed to lead to complete removal of a compound. Under anaerobic conditions, TCE biologically degrades via sequential	EPA removed the characterization of anaerobic biodegradation as "fast," instead noting that anareobic biodegredation occurs. In anaerobic environments, TCE biodegradation products include potentially hazardous substances including trichloroethylene, dichloroethene and vinyl chloride (Vogel and McCarty, 1985).

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	removal of chloride ions first to cis-dichloroethene, and next to vinyl chloride, which is itself a potent carcinogen. Vinyl chloride degradation to ethane (under anaerobic conditions) is often the rate-limiting step in this transformation, as it is mediated by a select group of microorganisms. As the rate-limiting step, there are many documented cases of stalled TCE-degradation, which has led to elevated vinyl chloride concentrations in the environment – arguably a condition as bad as or worse than TCE alone. • Where TCE is discharged into the environment, simply reporting standard biodegradation rates can obscure important impacts due to transformation processes.	
EPA should consider legacy uses		
98	**PUBLIC COMMENTS:** EPA should consider the legacy risks and exposures posed by TCE. To fulfill its statutory mandate, EPA must consider all forms of TCE's use and disposal. Failure to do so results in an incomplete accounting of the risks of injury TCE presents. Legacy exposure contributes to the rate of background exposure to individuals, and may result when people live or work in environments that contain legacy chemicals as well as when legacy disposals cause individuals to come into contact with a chemical substance through the air, water, or another exposure pathway. Cumulative exposures, including legacy exposures, increase the health risks faced by individuals and place a greater burden on subpopulations that have heightened sensitivity to TCE or face especially high exposures to it. • Legacy exposures to TCE are of particular concern in New York City due to the presence of TCE in detectable quantities in soil vapor and groundwater in many locations. The extent of exposure may be substantial in certain New York City neighborhoods given the vast historical use of this compound, its relative persistence in anaerobic conditions, and the variable age and condition of New York City buildings.	The use of TCE in the past are not "legacy" uses. As described in EPA's Risk Evaluation Rule (82 FR 33726 (July 20, 2017)), a legacy use is an ongoing use of a chemical substance in a particular application where the chemical substance is no longer being manufactured, processed, or distributed in commerce for that application. The example provided in the Rule is insulation, which may be present in buildings after a chemical substance component is no longer being made for that use. EPA has evaluated disposal as a condition of use and determined that it presents an unreasonable risk of injury to health. EPA has determined that general population exposures due to drinking water contamination, groundwater contamination, and air emissions are under the jurisdiction of other statutes administered by EPA and are outside the scope of this risk evaluation. In
104	**PUBLIC COMMENTS:**	

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	EPA is urged to consider the impacts of legacy use of TCE on tribal populations. The Ninth Circuit Court of Appeals ruled that EPA can no longer exclude "legacy" chemical uses from a risk evaluation, nor can it exclude any COUs from consideration. It also affirmed that the Toxic Substances Control Act (TSCA) "definition of 'conditions of use' clearly includes uses and future disposals of chemicals." Legacy use of products containing TCE was not considered in this draft risk evaluation. In order to accurately address the risks that TCE may pose to human health and the environment, environmental releases from unlined landfills containing it have to be evaluated. Not considering such environmental releases and the risks that they pose disproportionately affects tribes' exposures, in this case due to the unique disposal circumstances on tribal lands and in tribal communities.	exercising its discretion under TSCA section 6(b)(4)(D) to identify the conditions of use that EPA expects to consider in a risk evaluation, EPA believes it is important for the Agency to have the discretion to make reasonable, technically sound scoping decisions. EPA did not include legacy disposals, (*i.e.,* disposals that have already occurred), because they do not fall under the definition of conditions of use under TSCA section 3(4).

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2. Environmental Exposure and Releases

Environmental Exposure and Releases		
Charge Question 2.1: Please comment on the approaches, models, and data used in the water release assessment including comparison of modeled data to monitored data (Section 2.2). **Charge Question 2.2.:** Please provide any specific suggestions or recommendations for alternative data or estimation methods, including modeling approaches, that could be considered by EPA for conducting or refining the water release assessment and relation to monitored data (Section 2.2).		
#	**Summary of Comments for Specific Issues Related to Charge Question 2**	**EPA/OPPT Response**
Concerns with release modeling or comparison of model results to monitoring data		
SACC	**SACC COMMENTS:** Recommendation: Compare model estimates with values from municipal wastewater or National Pollutant Discharge Elimination System (NPDES) discharge data from industrial wastewater treatment facilities to determine model sensitivity. Modeling estimates were obtained from E-FAST using data compiled from TRI, DMR, and CDR. A probabilistic dilution module is then used to estimate surface water concentrations in freshwater streams and still water systems. • Several Committee members indicated that it is unclear how these data are used in the model. For example, it is uncertain how NPDES data from DMR are used. Based upon the draft risk evaluation, it seems that the only data compiled from DMR are dilution data. It is unclear why monitoring data for TCE in wastewater effluent was not obtained from NPDES. It seems that only the 10th percentile value of stream dilution is used from DMR and is considered a conservative estimate. • The Committee found it unclear why the upper end conservative (*i.e.,* 90th percentile) of E-FAST values are not used or why effluent values are not used. In fact, it appears that municipal wastewater measurements are excluded from the water quality exchange (WQX) measured data.	NPDES reporting data from DMR were not used for dilution factors in modeling. NPDES data were used for many releasing sites as the bases for the annual loading/release volumes that serve as the key inputs for the aquatic exposure model. Surface water concentrations are estimated using loading volumes (not effluent concentrations) with receiving water body stream flow. E-FAST (U.S. EPA, 2014c) surface water concentrations described as 10th percentile are the more conservative values. These are based on low-end (10th percentile) stream flow distributions for sites modeled using industry-specific stream flow distributions rather than known or estimated stream flow for a specific site. Therefore, use of the 10th percentile stream flow for receiving water bodies results in more conservative surface water concentration estimates for use in risk characterization. Surface water monitoring data from WQP were

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	• Concerns were expressed on the use of a model that is specifically designed for runoff scenarios, but spills and runoff are excluded from the draft TCE risk evaluation. • There is a lack of clarity regarding references to concentrations. For example, the range of measured surface water concentrations near facilities reported as 0.4-477 parts per billion (ppb) is not the observed concentration range. The observed range is ~0.05-9090 µg/L. As such, the text is misleading as written. • One Committee member thought that the approaches followed by EPA to assess water releases seemed adequate. This member thought that the draft risk evaluation did a good job in highlighting the limitations and uncertainties of the assessment. For instance, the TRI data are probably the best source for mass flows, but given its inherent limitations (*e.g.,* excluding companies with less than 10 full-time employees, minimum thresholds, potential underreporting), the Committee suggested that this is likely to be an underestimation of loading.	considered relevant for comparison with the modeled surface water concentrations in water bodies. E-FAST (U.S. EPA, 2014c) and its underlying models and equations have been peer reviewed and used to estimate surface water concentrations resulting from industrial point source releases for many years. The highest reported measured concentration level from Table 2-11 is 447µg/L, while the highest estimated/modeled concentration exceeds 9,000 µg/L (Tables 2-7 through 2-9, Appendix C). EPA has edited the titles of Tables 2-7 through 2-9 to clarify that these concentrations are estimated and not measured. EPA appreciates the feedback and this point related to potential underestimations based on TRI's minimum reporting thresholds is discussed in Section 2.2.6.3.
SACC	**SACC COMMENTS:** Recommendation: Compare E-FAST advantages and disadvantages with other models. In Section 2.2.3, the advantages of using EPA's E-FAST are listed. Several Committee members thought that to be fair to readers, at least one disadvantage to using this tool for everything should be listed. For example, using a model that does not consider the fate of the chemical is problematic. Members wondered if other models could be compared to the E-FAST results. • E-FAST does not estimate stream concentrations based on the potential for downstream transport and dilution. This implies that E-	Section 2.2.6.3 discusses the uncertainties associated with using E-FAST in this evaluation, including the disadvantages noted. EPA states "E-FAST 2014 estimates surface water concentrations at the point of release, without post-release accounting for environmental fate or degradation such as volatilization, biodegradation, photolysis, hydrolysis, or partitioning." In light of this shortcoming, EPA has conducted additional

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	FAST is acceptable for near-field environmental concentration estimation but not acceptable for estimating downstream concentrations, which are the bulk of environmental measurements. • E-FAST stream flow data are 15-30 years old. The draft risk evaluation needs more recent data (last 10 years) to significantly decrease uncertainty.	fate analysis for two sites with chronic COC (920 µg/L) exceedances (See Section 4.3.1 and 2.2.6.3). EPISuite fugacity modeling using WVOLWIN was conducted to inform the degree to which volatilization may impact the modeled stream concentrations estimated in E-FAST (U.S. EPA, 2014c). Parameters (wind speed, current speed, and water depth) reflective of two releasing sites with the highest predicted surface water concentrations (Praxair Technology Center in Tonawanda, NY and NASA Michoud in New Orleans, LA; see Table 4-1) were used to estimate TCE volatilization half-lives, which varied from one day to more than 10 years. The effect of volatility on estimating instream concentrations is expected to be highly variable and site-specific depending on stream flow and environmental conditions. For discharges to still, shallow water bodies, E-FAST estimates are less likely to overestimate surface water concentrations, as TCE is predicted to have a long half-life in such still water bodies. For discharges to faster-flowing, deeper water bodies, E-FAST estimates may inadequately reflect instream volatile losses expected within the timeframe of one day. Given this variation and the predicted half-life of TCE in flowing water bodies, E-FAST surface water concentrations may best represent concentrations found at the point of discharge. In Section 2.2.6.3, EPA addresses this point by

		stating "Additionally, E-FAST does not estimate stream concentrations based on the potential for downstream transport and dilution. These considerations tend to lead to higher predicted surface water concentrations. Dilution is incorporated, but it is based on the stream flow applied. Therefore, there is uncertainty regarding the level of TCE that would be predicted downstream of a releasing facility or after accounting for potential volatilization from the water surface, which is dependent on the degree of mixing in a receiving water body." The assumptions and uncertainties of the stream flow dataset within E-FAST, including the old age of the data, are discussed in Section 2.2.6.3.
Uncertainty in release estimates		
SACC	**SACC COMMENTS:** One Committee member thought that Table 2-10, although not a full uncertainty assessment, provides a good sense of the potential uncertainty through presenting data ranges and standard deviations.	EPA appreciates the feedback.
SACC	**SACC COMMENTS:** Recommendation: Discuss the potential uncertainties of other wastewater treatment processes (*e.g.,* aeration), particularly with volatile chemicals. • The estimated percent removal from wastewater treatment is based on a specific kind of industrial wastewater treatment facility (IWTF). Variation in types of IWTFs (sludge [dewatering], chemical, biological [aerobic, anaerobic, composting], physical [screening, sedimentation, skimming]) that manufacture or process TCE should be discussed. This is particularly important because aeration is typically used in secondary treatment. At a minimum, a	Possible uncertainties in the WWTP removal estimates include confidence in the physical-chemical properties, the range of reported aerobic biodegradation rates, and variation in performance among wastewater treatment plants. The physical-chemical properties reported in Table 1-1 and used in the STPWIN model are reported in high-quality data sources and align with expected values for TCE, and thus are of high-confidence. The uncertainty in

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	range of estimated removal percentages (or a confidence interval around the estimate of percent removal) should be provided.	biodegradation rates is discussed in Section 2.1.3, and TCE removal from wastewater by biodegradation was assessed to range from negligible to complete depending on the conditions in a given WWTP. The TCE removal performance may vary among WWTP, but the STPWIN model is designed to estimate removal from a model, conventional WWTP. The removal estimated by STPWIN for abiotic processes alone is 81%.
Geospatial/geographic analysis of releases concerns		
SACC	**SACC COMMENTS:** • Several Committee members expressed concerns about the geospatial analysis approach. If the geospatial analysis finds a Superfund site within 1-5 miles of the facility, then the draft risk evaluation indicated that those monitoring sites were excluded. • One Committee member was uncertain how Department of Defense (DOD) facilities that use TCE are treated. Of additional concern would be the possibility that the DOD facility also included a Superfund site. This member also had concerns for situations where the monitoring site is downstream (down slope) of the TCE use facility but upstream (up slope) from the Superfund site.	In Section 2.2.6.2.3, EPA states that the monitoring stations co-located with facilities in the same HUC in the 2016 set were also examined for proximity to Superfund sites; however, no Superfund sites were identified within five miles of these sites. While monitoring data from WQP/WQX clearly associated with superfund sites were not included in the monitoring data summary in Table 2-10, superfund sites were still considered in the GIS analysis to identify whether any of the observed concentrations may be associated with superfund sites rather than the scoped COUs. Facilities modeled were based on the scoped COUs and Occupational Exposure Scenarios (OES). Release sites were not excluded from the release and exposure assessment unless they were deemed not to fall within the scope of this evaluation.

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SACC	**SACC COMMENTS:** Geographic coordinates (p. 90): One Committee member thought that location of release points is needed rather than the "address" of the facility or the "front door" of the Superfund site. This member thought that the geographic analysis sounded quite cursory even though it is a screening analysis. This member also thought that incorporating land slope, Superfund site boundaries, and facility discharge points would not be that much extra work.	EPA appreciates the feedback on its GIS analysis in this evaluation and will consider how to make such analyses more robust.
SACC	**SACC COMMENTS:** Geographic information systems (GIS) work has not been validated through ground truthing.	
Release data and data presentation concerns		
SACC	**SACC COMMENTS:** Recommendation: Add a few explanatory paragraphs immediately after the concept of "cleansed data set." • Several Committee members pointed out that in the beginning of Section 2.2.6.2.2, it was unclear what 'cleansed data sets' means. The Committee recommended enhancing the clarity with a quick reminder of the definition, given the length of the overall report.	EPA has updated language in Section 2.2.4.2 and 2.2.6.2.2 to clarify what was meant by "cleansed" dataset. Section 2.2.4.2 now reads "The "Site data only" and "Sample results (physical/chemical metadata)" files were linked using the common field "Monitoring Location Identifier" and then filtered to eliminate records not relevant to the scope of the environmental evaluation. Specifically, filtering was applied to select the media of interest (*i.e.,* surface water), eliminate records that were quality control samples (*i.e.,* field blanks) or identified as having analytical quality concerns (*i.e.,* quality control issues, sample contamination, or estimated values), and eliminate records associated with contaminated sites (*i.e.,* Superfund)." Section 2.2.6.2.2 now refers to the "filtered" dataset rather than "cleansed."
SACC	**SACC COMMENTS:**	

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	One Committee member thought that the state of active facility releases and release characteristics should be reported in Section 2.2.2.2.2 or that Section 2.2.2.2.2 text should be moved or cross-referenced to pp. 92 and 93.	EPA will investigate either referencing or moving this information for improved clarity in future risk evaluations.
SACC	**SACC COMMENTS:** Table 2-10: One Committee member indicated that with such a high fraction of non-detect (ND) levels, the average is likely an overestimate of central tendency while standard deviation is likely an underestimate of variability. The member noted that in all years, the average of detections is less than the average of all data, suggesting that there are a lot of NDs from sites where the detection level is closer to 5 than to 0.022.	EPA added language addressing this point in the uncertainties discussion in Section 2.2.6.3.
SACC	**SACC COMMENTS:** A Committee member commented that the estimates of release days (Section 2.2.2.2.2.3) are really assumptions, not estimates. There are no data on exactly how these facilities operate. • 'Footnote a' to Table 2-2 assumes 260 days of operation per year in assessing annual releases from TRI and DMR data. But Appendix I apparently assumes and justifies the use of 350 operating days per year (see 'footnote c' to Table Apx I-2). The number of operating days that form the basis for the range of manufacturing estimated daily releases reported in Table 2-2 is not reported and is not clear in the associated text. Appendix I discusses the approach to estimating water releases from manufacturing sites using effluent guidelines in the situation where TRI and DMR data were not available or where TRI and DMR data did not sufficiently represent releases of TCE to water for a COU. • It would be useful to know what fraction of manufacturing sites had water releases that were estimated by this approach and what fraction used monitoring data directly. Similarly, it would be useful to know what fraction of processing facilities under each COU were represented by estimates and which by monitoring data. This has direct relevance on the uncertainty that would be assigned to the	EPA assessed releases from TCE manufacturing sites at 350 days per year based on assuming seven days per week and 50 weeks per year with two weeks per year for shutdown activities which is consistent with the information provided in Appendix I. Release days per year for other OES are discussed in Section 2.2.2.2.3. Footnote a refers to vapor degreasing OES. Information on release estimations versus monitoring data for manufacturing sites (as well as all other OES sites) are available in the Supplemental Information File: Environmental Releases and Occupational Exposure Assessment. Appendix I is meant to illustrate how releases were calculated for TCE manufacturing sites

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	range of estimates reported in Table 2-2 (this table should refer to Table 2-4 for clearer description of assumption on release days). • Difficulty justifying pounds per day values in Table 2-2 with kg/site-day estimates presented in Appendix I. • 'Footnote a' to Table 2-2 justifies using the Open Top Vapor Degreasers (OTVD) range of water releases for multiple other degreasing, cleaning, and metalworking applications because "releases were estimated using TRI and DMR data." This sounds less like a justification than an acknowledgement that there are only reliable water release data for larger OTVD operations.	where monitoring data were not available. The pounds per day values can be verified in the Supplemental Information File: Environmental Releases and Occupational Exposure Assessment. The days of water releases from all vapor degreasing OES were based on the 2017 ESD on the Use of Vapor Degreasing as shown in Table 2-4.
SACC	**SACC COMMENTS:** Recommendation: Incorporate an estimate for releases from all facilities that are likely to use TCE but that do not report TRI data. • Several Committee members recommended that EPA should incorporate an estimate for releases (via maximum likelihood, censored regression, or equivalent; see Helsel, 1990 and Helsel, 2005) from approximately 68,400 facilities that are likely to use TCE but that do not report TRI data. This approach uses the distribution of known observations to predict the unknown observations (non-detects). The draft risk evaluation lists 68,600 potential or likely users (Table 2-3). EPA states that reports are available from 183 facilities and 8 WWTPs. Data from these locations could be used to develop a population distribution that could be used to estimate total releases from all facilities.	EPA's analysis uses TRI (U.S. EPA, 2017g) and DMR (U.S. EPA, 2016a) to estimate the highest local per site water releases of TCE. EPA has added a mass balance analysis as suggested to Appendix R of the Risk Evaluation.
SACC	**SACC COMMENTS:** Recommendation: To be conservative, high percentile estimates of releases should be used anytime monitoring data are not available. • Several Committee members indicated that the exclusion of spills is inappropriate as spills result from TCE uses in commerce. One Committee member expressed concern that this decision is unprotective (*e.g.,* not appropriately conservative). • The impact of spills needs to be discussed. Several of the National	Spills and leaks generally are not included within the scope of a TSCA risk evaluation because in general they are not considered to be circumstances under which a chemical substance is intended, known or reasonably foreseen to be manufactured, processed, distributed, used, or disposed of. To the extent there may be potential exposure from spills and

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	Institute for Occupational Safety and Health (NIOSH) Health Hazard Evaluations (HHE) report that workers are concerned about the impact of spills and cleanup and that those are reported as associated with headaches, dizziness, and other symptoms.	leaks, EPA is also declining to evaluate environmental exposure pathways addressed by other EPA-administered statutes and associated regulatory programs. First, EPA does not identify TCE spills or leaks as "conditions of use." EPA does not consider TCE spills or leaks to constitute circumstances under which TCE is manufactured, processed, distributed, used, or disposed of, within TSCA's definition of "conditions of use." Congress specifically listed discrete, routine chemical lifecycle stages within the statutory definition of "conditions of use" and EPA does not believe it is reasonable to interpret "circumstances" under which TCE is manufactured, processed, distributed, used, or disposed of to include uncommon and unconfined spills or leaks for purposes of the statutory definition. Further, EPA does not generally consider spills and leaks to constitute "disposal" of a chemical for purposes of identifying a COU in the conduct of a risk evaluation. In addition, even if spills or leaks of TCE could be considered part of the listed lifecycle stages of TCE, EPA has "determined" that spills and leaks are not circumstances under which TCE is intended, known or reasonably foreseen to be manufactured, processed, distributed, used, or disposed of, as provided by TSCA's definition of "conditions of use," and EPA is therefore

		exercising its discretionary authority under TSCA section 3(4) to exclude TCE spills and leaks from the scope of the TCE risk evaluation. The exercise of that authority is informed by EPA's experience in developing scoping documents and risk evaluations, and on various TSCA provisions indicating the intent for EPA to have some discretion on how best to address the demands associated with implementation of the full TSCA risk evaluation process. Specifically, since the publication of the Risk Evaluation Rule, EPA has gained experience by conducting ten risk evaluations and designating forty chemical substances as low- and high-priority substances. These processes have required EPA to determine whether the case-specific facts and the reasonably available information justify identifying a particular activity as a "condition of use." With the experience EPA has gained, it is better situated to discern circumstances that are appropriately considered to be outside the bounds of "circumstances… under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of" and to thereby meaningfully limit circumstances subject to evaluation. Because of the expansive and potentially boundless impacts that could result from including spills and leaks as part of the risk evaluation (*e.g.,* due to the unpredictable and irregular scenarios that would need to be accounted for, including

		variability in volume, frequency, and geographic location of spills and leaks; potential application across multiple exposure routes and pathways affecting myriad ecological and human receptors; and far-reaching analyses that would be needed to support assessments that account for uncertainties but are based on best available science), which could make the conduct of the risk evaluation untenable within the applicable deadlines, spills and leaks are determined not to be circumstances under which TCE is intended, known or reasonably foreseen to be manufactured, processed, distributed, used, or disposed of, as provided by TSCA's definition of "conditions of use." Exercising the discretion to not identify spills and leaks of TCE as a COU is consistent with the discretion Congress provided in a variety of provisions to manage the challenges presented in implementing TSCA risk evaluation. See *e.g.,* TSCA sections 3(4), 3(12), 6(b)(4)(D), 6(b)(4)(F). In particular, TSCA section 6(b)(4)(F)(iv) instructs EPA to factor into TSCA risk evaluations "the likely duration, intensity, frequency, and number of exposures under the conditions of use….," suggesting that activities for which duration, intensity, frequency, and number of exposures cannot be accurately predicted or calculated based on reasonably available information, including spills and leaks, were not intended to be the

		focus of TSCA risk evaluations. And, as noted in the preamble to the Risk Evaluation Rule, EPA believes that Congress intended there to be some reasonable limitation on TSCA risk evaluations, expressly indicated by the direction in TSCA section 2(c) to "carry out [TSCA] in a reasonable and prudent manner." For these reasons, EPA is exercising this discretion to not consider spills and leaks of TCE to be COUs. Second, even if TCE spills or leaks could be identified as exposures from a COU in some cases, these are generally not forms of exposure that EPA expects to consider in risk evaluation. TSCA section 6(b)(4)(D) requires EPA, in developing the scope of a risk evaluation, to identify the hazards, exposures, conditions of use, and potentially exposed or susceptible subpopulations the Agency "expects to consider" in a risk evaluation. As EPA explained in the "Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act" ("Risk Evaluation Rule"), EPA may, on a case-by-case basis tailor the scope of the risk evaluation "in order to focus its analytical efforts on those exposures that are likely to present the greatest concern, and consequently merit an unreasonable risk determination." 82 FR 33726, 33729 (July 20, 2017).

		In the problem formulation documents for many of the first 10 chemicals undergoing risk evaluation, EPA applied the same authority and rationale to certain exposure pathways, explaining that "EPA is planning to exercise its discretion under TSCA 6(b)(4)(D) to focus its analytical efforts on exposures that are likely to present the greatest concern and consequently merit a risk evaluation under TSCA...." This approach is informed by the legislative history of the amended TSCA, which supports the Agency's exercise of discretion to focus the risk evaluation on areas that raise the greatest potential for risk. See June 7, 2016 Cong. Rec., S3519-S3520. In addition to TSCA section 6(b)(4)(D), the Agency also has discretionary authority under the first sentence of TSCA section 9(b)(1) to "coordinate actions taken under [TSCA] with actions taken under other Federal laws administered in whole or in part by the Administrator." TSCA section 9(b)(1) provides EPA authority to coordinate actions with other EPA offices, including coordination on tailoring the scope of TSCA risk evaluations to focus on areas of greatest concern rather than exposure pathways addressed by other EPA-administered statutes and regulatory programs, which does not involve a risk determination or public interest finding under TSCA section 9(b)(2). EPA has already tailored the scope of this risk evaluation using such discretionary

		authorities with respect to exposure pathways covered under the jurisdiction of other EPA-administered statutes and associated regulatory programs (see section 1.4.2). Following coordination with EPA's Office of Land and Emergency Management (OLEM), EPA has found that exposures of TCE from spills and leaks fall under the jurisdiction of RCRA. See 40 CFR 261.33(d) (defining in part a hazardous waste as "any residue or contaminated soil, water or other debris resulting from the cleanup of a spill into or on any land or water of any commercial chemical product or manufacturing chemical intermediate having the generic name listed [40 CFR 261.33(e) or (f)], or any residue or contaminated soil, water or other debris resulting from the cleanup of a spill, into or on any land or water, of any off-specification chemical product and manufacturing chemical intermediate which, if it met specifications, would have the generic name listed in [40 CFR 261.33(e) or (f)]"); 40 CFR 261.33(f) (listing TCE as hazardous waste no. U080). As a result, EPA believes it is both reasonable and prudent to tailor the TSCA risk evaluation for TCE by declining to evaluate potential exposures from spills and leaks, rather than attempt to evaluate and regulate potential exposures from spills and leaks under TSCA.

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		Releases from municipal landfills are regulated under RCRA. As explained in more detail in Section 1.4.2, EPA believes that coordinated action on exposure pathways and risks addressed by other EPA-administered statutes and regulatory programs is consistent with statutory text and legislative history, particularly as they pertain to TSCA's function as a "gap-filling" statute, and also furthers EPA aims to efficiently use Agency resources, avoid duplicating efforts taken pursuant to other Agency programs, and meet the statutory deadline for completing risk evaluations. EPA does not expect exposure to consumers from disposal of consumer products. It is anticipated that most products will be disposed of in original containers, particularly those products that are purchased as aerosol cans. As described in section 1.4.2 EPA is not evaluating on-site releases to land from RCRA Subtitle D municipal solid waste (MSW) landfills or exposures of the general population from such releases in the TSCA evaluation because they are adequately addressed by other EPA statutes. Disposal of household waste to municipal landfills is covered under the jurisdiction of RCRA as discussed in section 1.4.2.
SACC	**SACC COMMENTS:** Recommendation: EPA should consider the impact on discharge estimates of multiple facilities discharging to a single publicly-owned treatment work (POTW).	The STPWIN model assumes an influent concentration of 10 µg/L flow at 1,000,000 L/hr (6.3 millions of gallons per day) (Clark et al.,

	• In evaluating Appendix P, one Committee member concluded that releases from degreasing operations were estimated based on "best practices" for OTVDs. Under this approach, 80% of wastewater is released to a water treatment facility. If this assumption is made, the Committee member concluded that aggregates from all commercial users within a water treatment district could discharge to a single POTW. • Data presented in the draft risk evaluation did not allow determination of the extent to which multiple facilities were discharging to a single facility and if the magnitude of any such discharges would be essential to estimate high centile releases from POTWs receiving TCE from multiple commercial users.	1995). This equates to 0.24 kg/day of TCE entering the model treatment plant. The estimated daily water releases reported in Table 2-2 of the Risk Evaluation ranged from 2.53E-07 to 24.1 kg/site-day. Therefore, the STPWIN model covers most of the estimated daily water releases except for those at the higher range which exceed the mass loading considered in STPWIN. The maximum amount of TCE that could be removed by volatilization is 100,000 kg/day, which is based on the 8960 g/m3 air flow in the STPWIN model aeration. From this analysis the STPWIN model predicted TCE removal of 80% by volatilization likely covers the aggregate discharge from multiple facilities.
SACC	**<u>SACC COMMENTS:</u>** Recommendation: The Committee restated the need for robust monitoring data to be used in exposure assessments. • One Committee member concluded that the hydrologic unit code approach can be valuable if and only if assessments can show that measurements at downstream monitoring sites are predictive of discharges from upstream facilities. Otherwise, the Committee member expressed concern that the approach is likely to underreport TCE concentrations downstream of manufacturing facilities.	For this evaluation, EPA utilized data from the Water Quality Portal (WQP), which integrates publicly available US water quality data from multiple databases: 1) the United States Geological Survey National Water Information System (USGS NWIS); 2) EPA's STOrage and RETrieval (STORET); and 3) the United States Department of Agriculture Agricultural Research Service (USDA ARS) Sustaining The Earth's Watersheds - Agricultural Research Database System (STEWARDS). EPA also conducted a full systematic review to identify surface water monitoring data from peer reviewed literature and grey literature sources. EPA appreciates the feedback on its GIS analysis and co-location analysis using HUCs.

		However, since modeled releases are site-specific and associated with scoped COUs, resultant surface water concentration estimates may or may not be near or associated with sampling sites with measured data from national or peer reviewed data sources.
SACC	**SACC COMMENTS:** Tables 2-7 to 2-9: Several Committee members thought that the aqueous concentrations should be consistently expressed as mg/L.	Concentrations in Tables 2-7 through 2-9 are now consistently expressed in µg/L units, aligning with units in Tables 2-10, and 2-11.
108	**PUBLIC COMMENTS:** EPA appears to have made no significant effort to identify data on the TCE in soil or sediment, available for example in EPA's STORET database, which it used to obtain surface water data on TCE, despite the fact that EPA does mention in passing that "[l]imited sediment monitoring data … suggest that TCE is present in sediments." EPA did conduct such searches and located substantial amounts of data for another chemical undergoing risk evaluation (methylene chloride). There is every reason to believe that analogous data for TCE would have been located had EPA conducted the same kinds of searches it did for methylene chloride.	As shown in the conceptual model in Figure 1-6, soil and land-applied biosolid exposure compartments are indicated as being associated with pathways not further analyzed based on work done during problem formulation. The systematic review process for identifying, screening, and evaluating data was tailored based on these decisions. However, in response to SACC comments, EPA added a quantitative assessment of sediment-dwelling organisms using E-FAST (U.S. EPA, 2014c) results and aquatic invertebrate data to the TCE risk evaluation in Section 4.1.3.
Eco exposure pathways included are incomplete or not relevant		
103	**PUBLIC COMMENTS:** EPA should clarify the purpose of evaluating acute environmental risks. Typically, acute environmental risks would be characterized to represent a large, sudden environmental exposure such as a spill. The COUs evaluated represent continuous, regular releases, which are characteristic of a chronic exposure.	Acute environmental risks are considered because there is uncertainty around the frequency of environmental releases. The assumptions were made that each facility would release their total volume of TCE to surface

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		water over 20 days and over a maximum number of days (*e.g.,* 260 days, 350 days depending on the exposure scenario). Because EPA does not know the exact number of days over which the environmental release occurs, EPA found it essential to assess acute environmental risk.
108	**PUBLIC COMMENTS:** EPA dismissed potential exposure based on land-applied biosolids (p. 90), stating that: "TCE was not detected in EPA's TNSSS, nor was it reported in biosolids during EPA's Biennial Reviews for Biosolids…" (U.S. EPA, 2019d). However, our review of the cited document as well as the TNSSS Sampling and Analysis Technical Report did not indicate that TCE was included in the sample analysis, which calls into question use of the biennial review as support for EPA's conclusions. TCE has been detected in biosolids at concentrations as high as 8,770 µg/kg. • A recent Office of Inspector General (OIG) report indicates EPA "lacks the data or risk assessment tools" to make determinations on the risk levels for pollutants found in biosolids. According to the OIG, "[t]he regulations for biosolids do not require the EPA to obtain the data necessary to complete risk assessments." • EPA states that "[u]sing reasonably available information, exposures will be estimated (usually quantitatively) for the identified conditions of use." EPA cannot prepare an accurate quantitative estimate for exposure if EPA has excluded exposure pathways. "For environmental evaluations specifically, EPA plans to include a discussion of the nature and magnitude of the effects, the spatial and temporal patterns of the effects, [and] implications at the species, population, and community level" (82 Fed. Reg. at 33,743). EPA cannot accurately discuss the magnitude of the effects on the environment or the spatial and temporal patterns of those effects if EPA ignores the vast majority of the environmental exposures, as EPA proposes to do.	EPA based its decision not to further evaluate TCE exposure via land-applied biosolids in the Risk Evaluation on fate properties; in particular, TCE is not anticipated to partition to biosolids during wastewater treatment. Any TCE present in the water portion of biosolids following wastewater treatment and land application would be expected to rapidly volatilize into air.

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	• EPA did not conduct a significant analysis of biosolids in the draft risk evaluation; EPA instead dismissed this pathway on the basis of physical-chemical and fate properties of TCE. EPA should obtain some monitoring data to confirm these analyses, but in any event, EPA cannot rationalize ignoring exposures from biosolids on the basis that TCE will enter the water and air and then also choose to ignore the exposure pathways through water and air. EPA's justification for ignoring the biosolids pathways for TCE highlights that EPA's decision to ignore other pathways is particularly arbitrary and capricious.	
EPA should consider background releases to the environment		
49, 99 56, 108	**PUBLIC COMMENTS:** The draft ignores the human health implications of TCE releases to the environment. TCE air emissions and contaminated groundwater, drinking water, and soil are pervasive across the United States. • By considering only water releases, EPA ignored the 48,245 pounds of TCE released on-site for land disposal. Updated TRI data from 2018 show that "other" TCE releases to land totaled nearly 157,000 pounds. This release appears to be from a single facility that seems to have been discharging TCE to land for a number of years. It is unclear how this facility is permitted for such a discharge. • EPA has given TRI and DMR data a "medium" confidence rating due to potential underreporting. Hence, the data cited above likely understate the extent of discharges of TCE to the environment. • For EPA to dismiss environmental impacts to soil and sediment based on predicted environmental partitioning does not represent consideration of the best available science or reasonably available information.	EPA acknowledges that it did not consider background exposure from the environment that workers, ONUs, consumers, or bystanders using products containing TCE might be exposed to in addition to exposures from the evaluated conditions of use. There is insufficient information reasonably available related to the likelihood of this scenario or the relative distribution of exposures from each pathway. This may result in an underestimation of risk, and EPA acknowledges that risk is likely to be elevated for individuals who experience TCE exposure in multiple contexts. Additional discussion of this issue has been added to Sections 2.3.2.6.1, 2.3.2.2.1, and 4.4.2. Emissions to ambient air from commercial or industrial stationary sources, or inhalation exposures of terrestrial species are covered under the jurisdiction of the Clean Air Act (CAA).

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		The assumptions and uncertainties associated with using TRI and DMR data sources, such as limitations on required reporters, are discussed in Sections 2.2.6.3 and 4.3. For sediment-dwelling organisms, during problem formulation, EPA determined that an insignificant portion of TCE is available to enter the sediment compartment. Therefore, while the sediment pathway was included, EPA did not plan to further analyze exposure to sediment-dwelling species, and in the draft risk evaluation, sediment-dwelling organisms were only assessed qualitatively. However, in response to SACC comments a quantitative assessment of sediment-dwelling organisms was added to the final TCE risk evaluation in Section 4.1.3. For terrestrial organisms, during problem formulation exposure pathways to these organisms through water and biosolids were within scope, but not further analyzed, because physical-chemical properties do not support these pathways. The land-applied biosolids pathway is within the scope of the risk evaluation, but during problem formulation EPA determined risks would not be quantitatively evaluated for land-applied biosolids because based on fate properties, TCE is not anticipated to partition to biosolids during wastewater treatment. Any TCE present in the water portion of biosolids following

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		wastewater treatment and land application would be expected to rapidly volatilize into air. And the air exposure pathway from biosolids and surface water are insignificant. Based on the Guidance for Ecological Soil Screening Levels (EPA, 2003a, b) document, for terrestrial wildlife, relative exposures associated with inhalation and dermal exposure pathways are insignificant, even for volatile substances, compared to direct ingestion and ingestion of food (by approximately 1,000-fold). In addition, TCE is not expected to bioaccumulate in tissues, and concentrations will not increase from prey to predator in either aquatic or terrestrial food webs. EPA has added language to the final risk evaluation document in Section 4.1.4 explaining this rationale. For terrestrial organisms, pathways that were out of scope include ambient air from industrial sources, disposal in landfills, incineration units, and underground injection. Environmental exposure pathways covered under the jurisdiction of other EPA-administered statutes and regulatory programs are not within the scope of the risk evaluation. Emissions to ambient air from commercial and industrial stationary sources, and associated inhalation exposures of terrestrial species, are covered under the jurisdiction of the Clean Air Act (CAA). Pathways from disposal to sediment, soil, water, and air are covered under Resource Conservation and Recovery Act (RCRA),

		CAA's Maximum Achievable Control Technology (MACT), and the Safe Drinking Water Act (SDWA). Clarifying language about what pathways are addressed under other statutes has been added to Section 1.4.2 of the Risk Evaluation.
49, 99	**PUBLIC COMMENTS:** TRI requirements apply to a narrow subset of facilities that release chemicals to the environment and thus understate total emissions. For example, the 2011 EPA National Emission Inventory (NEI) estimated U.S. TCE emissions of 3,250 tons – or 7,150,000 pounds, compared with the only ~2 million pounds indicated by TRI in 2017.	NEI is compiled every 3 years for the purpose of supporting residual risk evaluations as required by NESHAPs. NEI contains air emission estimates, which can be estimated by sites using a variety of methods, such as emission factors, mass balance, and stack monitoring. Purchase and disposal records are not reported to NEI. However, EPA was unable to use NEI data to reasonably estimate water releases as it only includes air releases from larger facilities and would not include releases from many smaller shops that use TCE.
49, 99	**PUBLIC COMMENTS:** TCE is frequently found at contaminated sites, resulting in contamination of groundwater and release of TCE vapors into ambient air and buildings. This is a significant concern at contaminated sites within the purview of the EPA Superfund program. Given the ubiquity of TCE in soil and groundwater, there are assuredly far more sites with TCE contamination than are identified. At these sites, volatilization of TCE from contaminated soils is relatively rapid and may lead to elevated ambient air levels in nearby communities.	EPA evaluated and considered the impact of existing laws and regulations (*e.g.,* regulations on landfill disposal, design, and operations) in the problem formulation step to determine what, if any future analysis might be necessary as part of the risk evaluation. During problem formulation EPA analyzed the TRI data and examined the definitions of elements in the TRI data to determine the level of confidence that a release would result from certain types of disposal to land (*e.g.,* RCRA Subtitle C hazardous landfill and Class I underground Injection wells) and incineration. EPA also

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		examined how TCE is treated at industrial facilities. EPA did not include emissions to ambient air from commercial and industrial stationary sources, which are under the jurisdiction of and addressed by Section 112 of the Clean Air Act. EPA did not include emissions to ambient air from municipal and industrial waste incineration and energy recovery units in the risk evaluation, as they are regulated under section 129 of the Clean Air Act. EPA did not include disposal to underground injection, RCRA Subtitle C hazardous waste landfills, RCRA Subtitle D municipal solid waste (MSW) landfills, and on-site releases to land from industrial non-hazardous waste and construction/demolition waste landfills in this Risk Evaluation. EPA did not include Superfund on-site releases to the environment, as they are under the jurisdiction of CERCLA. These methods of disposal fall under the jurisdiction of and are addressed by other EPA-administered statutes and associated regulatory programs.
56, 108	**PUBLIC COMMENTS:** • EPA cannot ignore environmental releases of a chemical because it cannot attribute each release to a particular COU. EPA has indicated that "only a few USGS-NWIS and STORET monitoring stations aligned with the watersheds of the TCE-releasing facilities identified under the scope of this assessment, and the co-located monitoring stations had samples with concentrations below the detection limit; therefore, no direct correlation can be made between them." • This language suggests that EPA may believe it must be able to	EPA has considered all identified measured surface water monitoring data regardless of whether it can be traced back to a specific COU. The GIS analysis was not conducted to exclude any of the measured data, but to identify potential associations between modeled and measured data, where possible. However, regardless of the outcome of the GIS analysis, monitoring data were considered for exposure

	attribute every environmental release of a chemical to a particular COU or facility in order to consider its risks in a risk evaluation. Nothing in TSCA allows EPA to ignore data simply because they have not been tied to a particular COU, let alone a particular facility. EPA must conduct risk evaluations under TSCA that consider all "reasonably available" information relating to a chemical substance, including information that may not be tied to specific COUs. • EPA is ignoring exposures from other COUs, such as "manufactur[ing]," "process[ing]," and potentially distribution in commerce, by for example ignoring the emissions from the manufacturing and processing facilities.	and risk characterization. Regarding exposures from COUs such as manufacturing, processing, and distribution in commerce, EPA has evaluated those conditions of use. EPA described background exposure in the uncertainties section acknowledging that the risk estimations in the Risk Evaluation may be underestimations, because background exposures and risk are not incorporated to the risk estimations for each COU. Emissions to ambient air from commercial or industrial stationary sources, or inhalation exposures of terrestrial species are covered under the jurisdiction of the Clean Air Act (CAA).
104	**PUBLIC COMMENTS:** EPA is strongly urged to consider environmental release from waste management sites, including transfer sites, construction and demolition sites, materials recovery facilities, and Subtitle D landfills. These should be evaluated with consideration of unlined facilities with resulting leachate subsurface flow, ponded water, direct surface water, and snowmelt runoff; ambient emissions from uncovered disposal areas; and untreated waste burning emissions.	Releases from landfills were not included in the risk evaluation as landfills are under the jurisdiction of RCRA (see section 1.4.2 of the risk evaluation).
105	**PUBLIC COMMENTS:** "Conditions of use" must certainly include releases into air, water, waste sites, and food, as these releases are inseparable from the use of a chemical. • EPA provides no analysis whatsoever as to: the extent to which the standards or criteria cover the full range of exposure to the chemical through the pathway; the extent and magnitude of releases of the chemical allowed under each of the regulatory standards or criteria; or any other factors that would be necessary to analyze to determine	The conceptual models only included exposure pathways that are within the scope of the risk evaluation. The environmental exposure pathways covered under the jurisdiction of other EPA-administered statutes and regulatory programs are not within the scope of the risk evaluation. As explained in more detail in Section 1.4.2 of the Final Risk Evaluation, EPA

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	the extent and nature of potential risk allowed under the standards. By not considering these releases, EPA is effectively reducing this substantial amount of TCE released into the environment to zero.	believes it is both reasonable and prudent to tailor TSCA Risk Evaluations when other EPA offices have expertise and experience to address specific environmental media, rather than attempt to evaluate and regulate potential exposures and risks from those media under TSCA. EPA believes that coordinated action on exposure pathways and risks addressed by other EPA-administered statutes and regulatory programs is consistent with statutory text and legislative history, particularly as they pertain to TSCA's function as a "gap-filling" statute, and also furthers EPA aims to efficiently use Agency resources, avoid duplicating efforts taken pursuant to other Agency programs, and meet the statutory deadline for completing Risk Evaluations. EPA has therefore tailored the scope of the Risk Evaluation for TCE using authorities in TSCA Sections 6(b) and 9(b)(1).
Confidence in release/discharge/spill data		
SACC	**SACC COMMENTS:** Recommendation: Clarify how confidence is assessed on overall release estimates. • The Committee noted that everything is assessed as having "medium" confidence in the summary of overall confidence in release estimates. It was not clear to the Committee that there are any rules as to what qualifies as "high" or "low." There seems to be a lot of uncertain components that go into a "medium" confidence assessment. Specifically, the Committee thought that the "medium" confidence for Commercial Printing and Copying is unjustified based as it is on one facility that is likely not representative of the whole industry. This should be an example of a "low" confidence occupational exposure scenario (OES) water release estimate.	Confidence in release estimates are thoroughly explained in Section 2.2.2.3.1. The assumptions and uncertainties associated with using TRI and DMR data sources, such as limitations on required reporters, are discussed in Section 4.3.1. Table 2-11 provides the full reported range of surface water concentrations from all but two of the identified data sources. Therefore, the high-end of measured ambient water TCE levels is shown regardless of whether the source

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	• A Committee member recommended that the Not Reported values in draft risk evaluation Table 2-11 be replaced with values calculated using the data in the source publications (an example table is provided). These publications contain ambient air data that show significant concentrations near manufacturing facilities. Another example table shows extracted data from U.S. EPA (1977) that were used to compute statistics. The same should be able to be done for data from other sources, especially federal documents, or publications from researchers at federal laboratories. • One Committee member commented that the draft risk evaluation does not adequately explain why historical measured concentrations of TCE are not considered representative of current releases (p. 95, lines 671-675 and p. 99, lines 787-792). • Another Committee member noted that the reduction in TCE use and process modifications over the last four decades make use of historical concentrations in the risk evaluation problematic.	reported central tendency estimates, which are sometimes shown in the Table as Not Reported. For the two data sources that did not report a full range of measured concentrations, the reported central tendency values are shown. EPA states that "These samples were collected in 1976-1977 near facilities producing and/or using methylchloroform, thus the concentrations reflect historical levels of TCE and are not considered to be representative of current conditions." Methylchloroform production is not included as a condition of use in this evaluation.
SACC	**SACC COMMENTS:** Modeling of TCE concentrations in river water is highly problematic without downstream monitoring data to parameterize modeling efforts. This would require both near and intermediate distances from facilities. • A Committee member noted that the draft risk evaluation does not use physiologically based pharmacokinetic (PBPK) models for fetal transfers and suggested that this may reflect a lack of data to parameterize those models. The same criteria should be used here, and if there are no data for model parameterization, conservative assumptions should be used throughout the draft risk evaluation. According to the Committee member, these conservative assumptions include the 1977 data, use of high centile concentrations, and inclusion of lower centile of degradation. None of these conservative considerations have been included in the draft risk evaluation. • Other Committee members commented that volume or use patterns do not consider any handling procedures, process, or engineering	The assessment is based on the reasonably available data regarding volume, use patterns, handling procedures, process or engineering changes. Conservative assumptions are used in the evaluation of aquatic exposures and are described in Sections 2.2.3 and 2.2.6.3. For example, a low-end estimate for days of release (*i.e.,* 20 days) is included for direct releasers. Additionally, the model itself does not incorporate downstream transport or post-release degradation or loss mechanisms such as volatilization.

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	changes that may have taken place over the intervening years, particularly after regulatory limits were enacted.	This point is acknowledged in Section 2.2.6.3 as a primary uncertainty associated with the E-FAST model (U.S. EPA, 2014c). Language has been added following additional fugacity modeling, which is discussed in Section 4.3.1: "The effect of volatility on estimating instream concentrations is expected to be highly variable and site-specific depending on stream flow and environmental conditions. For discharges to still, shallow water bodies, E-FAST estimates are less likely to overestimate surface water concentrations, as TCE is predicted to have a long half-life in such still water bodies. For discharges to faster-flowing, deeper water bodies, E-FAST estimates may inadequately reflect instream volatile losses expected within the timeframe of one day. Given this variation and the predicted half-life of TCE in flowing water bodies, E-FAST surface water concentrations may best represent concentrations found at the point of discharge. Despite these uncertainties, E-FAST is considered an appropriate screening model for near-field environmental concentrations."
SACC	**SACC COMMENTS:** Recommendation: More detailed GIS modeling is needed to raise confidence to moderate. • The draft assessment concludes overall moderate confidence in Aquatic Exposure Scenarios. Many on the Committee concluded that despite a lot of work and best intentions, confidence in exposure scenarios is low, primarily due to high propagation of uncertainties. More detailed GIS modeling is needed to raise confidence to moderate.	EPA will consider how to bolster such GIS analyses in future evaluations; however, some additional fugacity modeling was conducted and is presented in the final risk evaluation to address some of the primary uncertainties associated with E-FAST modeling, *i.e.,* the inability to incorporate downstream transport and fate processes such as volatilization. Please

		see Sections 2.2.6.3 and 4.3.1 for a description of the fugacity modeling using WVOLWIN within EPISuite and findings.
SACC	**SACC COMMENTS:** • Using notes from Supplemental Document 10_Environmental Data Extraction, one Committee member noted that data from the Lake Charles PPG Facility released TCE that produced mean surface water concentrations of 282 µg/L and median of 353 µg/L (U.S. EPA, 1977). Surface water concentrations at the Dow plant in Freeport, TX, ranged from 0.9 to 126 µg/L. • The table of environmental monitoring studies in Supplemental Document 10 reports ranges and standard deviations. In reporting the number of samples and detection frequencies in column 4 of the table, a value of 1 indicates that all samples had detectable concentrations. This is not completely clear, because it could also be read as there being only one sample with a detectable concentration in the sample.	EPA appreciates this feedback on the supplemental file. The detection frequency reported in parentheses reports the frequency or rate and not the number of samples with detections. For consistency with the other published risk evaluations, this column header is retained; however, EPA will consider clarifying this column header in future evaluations.
SACC	**SACC COMMENTS:** The Committee noted that Section 2.2.6.2, lines 567-572 has no mention of Appendix P, suggesting there is no way to determine the adequacy of the underlying information upon which surface water concentrations are based (Tables 2-7, 2-8, and 2-9). The Committee concluded that Appendix P contains assumptions that are not conservative and are improper for use in the absence of measured data for releases from commercial operations.	Cross-references to Section 2.2.2.1 and Appendix Q (formerly Appendix P) containing details on facility release data have been added to Section 2.2.2.6. Release estimates are based on reasonably available information obtained from the Toxics Release Inventory, Discharge Monitoring Report, National Emissions Inventory, Chemical Data Reporting, Effluent Limitation Guidelines, and Emission Scenario Documents.
Alternative data/approaches for release estimates are recommended		
SACC	**SACC COMMENTS:** Recommendation: Use NPDES data to confirm E-Fast outputs for TCE. • NPDES measurements of TCE from permit-required sampling	NPDES data were used for many releasing sites as the bases for the annual loading/release

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	results and notifications to state/EPA of compliance or noncompliance should be obtained. These data would allow a much more robust method of comparison of modeled E-FAST data versus measured data to be performed. While measured data are obtained from the WQX, these data are primarily surface water measurements that are rarely obtained from discharge sites where TRI or other input data are used in E-FAST. • The Committee expressed concern that available monitoring data could not be used to corroborate the monitoring approach given the downstream distance, which may represent an opportunity for EPA to implement a program of monitoring that can provide more data with greater confidence.	volumes that serve as the key inputs for the aquatic exposure model. Surface water concentrations are estimated using loading volumes (not effluent concentrations) with receiving water body stream flow. Release estimates and modeled concentrations in receiving water bodies are based on the scoped conditions of use, while monitoring data obtained from the WQP and/or peer-reviewed or grey literature sources are not. Therefore, there may or may not be a relevant proximity between the modeled surface water concentrations and the sampling sites with measured data obtained through systematic review.
SACC	**SACC COMMENTS:** Recommendations: (1) Clarify the use of ranges in number of facilities in Table 2-3. (2) Range estimates or a statement of uncertainty should be provided on the number of facilities for each OES. • A Committee member questioned the use of ranges in number of facilities in Table 2-3. For example, line 2 of the table reports 5 to 440 facilities that are in the scenario "Processing as a Reactant." Is one to assume that this means that EPA acknowledges that they are not sure of the number of facilities? Does this mean something like "we know of 5, and there could be as many as 435 or more facilities that do this?" • In Table 2-3 where the summary of estimates for the number of facilities for each OES are provided, one Committee member thought that the estimation of the number of facilities could be enhanced by adding a sense of uncertainty ± X percent or X facilities. This member thought that these data are evidently needed, as one sees the number of facilities for "processing as reactant"	The range provided for the number of sites from Processing as a Reactant is a function of known sites for this OES from TRI (U.S. EPA, 2017g) and DMR (U.S. EPA, 2016a) data and integrating it with sites reporting NAICS codes for this type of use. EPA acknowledges the uncertainties associated with these data in Section 2.2.2.3 of the Risk Evaluation.

	estimated at "5 to 440," which is quite a range, whereas the rest of the estimations are left without any measure of uncertainty.	
SACC	**SACC COMMENTS:** One Committee member could not find the surface water concentration maps mentioned in Section 2.2.5. This member was concerned that the color coding is provided but was not certain that the maps were found in Section 4 of the draft risk evaluation. If so, this member could not see the immediate reference.	EPA has addressed this point by including the referenced maps into Section 2.2.6.2.3.
SACC	**SACC COMMENTS:** In Figure 2-4, one Committee member thought that the choice of a tornado graph is not the best one to promote clarity and suggested that a set of pie charts or a sectioned bar graph may better illustrate the point.	EPA has addressed this point by removing the tornado plot and clearly describing the pictured observations in text (see Section 2.2.6.2.1).
SACC	**SACC COMMENTS:** Recommendation: Perform a sensitivity assessment for environmental exposures. Given the uncertainties and medium confidence ranking for the environmental exposure and releases, a sensitivity assessment is needed to better understand the impact of key assumptions and limitations in the final conclusions. • The Committee noted the inclusion of a sensitivity assessment performed on species (species sensitivity distribution [SSD] in Section 3), which is a good step forward. • Some Committee members recommended including an evaluation of how sensitive the environmental exposure estimations are to the assumptions, or at least provide a semiqualitative assessment.	Section 2.2.6.3 discusses the key sources of uncertainty in the aquatic exposure modeling. The key inputs driving exposure estimations are the release volume input (kg/site-day), the days of release, and the stream flow of the receiving waterbody. Section 2.2.2.3 and Table 2-5 outline sources of uncertainty and confidence in two of those key inputs: release days and release volumes.
SACC	**SACC COMMENTS:** • Several Committee members noted that the draft risk evaluation indicates that when it is not possible to confidently assign a facility to a specific COU based on TRI or DMR reporting information, it is assigned to its "most likely" or "primary" COU. It is not clear why the facilities were not asked for more information on how TCE is used on site. This seems reasonable, for example, for the manufacturing sites, where only three or maybe five are identified.	As noted in the document entitled EPA's Responses to Public Comments Received on the Scope Documents for the First Ten Chemicals for Risk Evaluation under TSCA, (EPA-HQ-OPPT-2016-0723-0067), EPA conducted extensive and varied data gathering activities for each of the first 10 chemicals,

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	• One member suggested that this approach be used to reduce uncertainty by obtaining information on the days of manufacture versus assuming 350 days/year for all.	including: • Extensive and transparent searches of public databases and sources of scientific literature, government and industry sector or other reports; • Searches of EPA TSCA 8(e), Chemical Data Reporting, and other EPA information holdings; and CBI submission holdings; • Searches for Safety Data Sheets (SDSs) using the internet, EPA Chemical and Product Categories (CPCat) data, the National Institute for Health's (NIH) Household Product Database, and other resources in which SDS could be found; • Preparation of a market analysis using proprietary databases and repositories; • Outreach meetings with chemical manufacturers, processors, chemical users, non-governmental organizations, trade organizations, and other experts, including other State and Federal Agencies (*e.g.,* Dept of Defense, NASA, OSHA, NIOSH, FDA and CPSC); and • Publication of conditions of use documents, scope documents, and problem formulation documents to solicit information generally from industry, nongovernmental organizations, and the public.
SACC	**SACC COMMENTS:** Recommendation: Link the National Hydrological Dataset to E-FAST. • Several Committee members noted that material flows are not the same as in the E-FAST database. The Committee recommended that a mass balance approach would be helpful to address some issues in	EPA has added a mass balance analysis as suggested to Appendix R of the Risk Evaluation to provide come context when comparing TCE production and releases.

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	comparing TCE production and releases. Several Committee members recommended that EPA link the National Hydrological Dataset to E-FAST.	EPA will consider updating its stream flow database or using the more recent sources for stream flow distributions in future evaluations to address this point.
SACC	**SACC COMMENTS:** Recommendation: Provide separate Supplement for EPI Suite™ data or change the title of the current supplement. • The supplemental PDF document, "5_TCE-Data Extraction for Environmental Fate and Transport Studies Public" (U.S. EPA, 2020) discusses results and assigns data quality for studies from which the input parameters used in EPI Suite™ are obtained. It also presents some EPI Suite™ model output. This is not clear from the document title, yet this is key information for draft risk evaluation readers.	The supplemental file in question is data extraction, which includes data obtained either from identified studies or from modeling results.
SACC	**SACC COMMENTS:** Recommendation: The implications of the Fugacity Level 3 modeling needs to be better explained. EPI Suite™ consists of several models. Some are used to predict physical-chemical properties, one is used to predict removal from WWTPs and another is the Fugacity Level 3 model. In some cases, they are linked, and in others, they are not. For example, physical-chemical properties can be manually added or estimated within EPI Suite™, then used in the STP model or fugacity models. • One Committee member concluded that the fugacity model predicts TCE movement from air to water, not water to air (p. 30; U.S. EPA, 2020b). The member noted that any consideration of TCE degradation in wastewater will only lower the initial concentration released to water and increase the predicted air-to-water flux. • Several Committee members thought that this was a serious flaw in the draft risk evaluation's assessment of environmental fate data (see Table 2-1 provided in the SACC report). The Committee suggested that this pertains to all chlorinated solvent TSCA risk assessments.	EPA ran the level III fugacity model in EPISuite™ (U.S. EPA, 2012b) using emissions from a mass balance developed to account for the amount of TCE entering and leaving all facilities in the United States. For the mass balance EPA attempted to quantify the amount of trichloroethylene associated with each of its life cycle stages from introduction into commerce in the U.S. (from both domestic manufacture and import), processing, use, release, and disposal. The results of the modeling are presented in Appendix S. Discussion of assumptions and uncertainties associated with TCE level III fugacity modeling and the SACC level III fugacity modeling results is presented in 2.1.3 Assumptions and Key Sources of Uncertainty for Fate and Transport.

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	• Several Committee members suggested that the ratios and mass loadings assumed in the default Fugacity Level 3 (fugacity model) within EPI Suite™ do not represent the draft risk evaluation's estimates of environmental releases (problem formulation Table 2-7). Default assumptions are 1000 kg/hour release of the chemical being evaluated into the compartments of air, water, and soil. More refinement of fugacity model within EPI Suite™ estimates can be done by using data from problem formulation Table 2-7 (U.S. EPA, 2018). The draft risk evaluation for TCE did not list estimates for total TCE releases to water or any other media. Therefore, the problem formulation contains the most comprehensive summary of the data available to estimate TCE releases to the environment. Data from problem formulation Table 2.7 (U.S. EPA, 2018) show annual TCE releases to air, water, and soil of 1,881,000, 52, and 50,000 pounds, respectively (the SACC only lists the higher mass numbers to the nearest 1000 pounds). There are also 2016 DMR data that show that 1,564 pounds of TCE released from the top 10 TCE producers (problem formulation 2.3.4, p. 34, last line).	
SACC	**SACC COMMENTS:** The SACC report provides a table including six scenarios to demonstrate using environmentally realistic release ratios of TCE to air, water, and soil that multimedia models such as EPI Suite™ show TCE moving from air to water, not from water to air. • Scenario 1 (Default): The default case, which shows equilibrium TCE concentrations in water that exceed releases to water by 63%. • Scenario 2 (Scaled Default): Retains the equal ratios of the default case but scaled to the total releases to all compartments (problem formulation Table 2-7). This scenario is provided to show that as long as the ratios released into the three compartments are the same, the relative distributions are predicted to be the same. • Scenario 3 (problem formulation): Shows the release rates to each compartment as calculated from Problem Formulation Table 2-7	EPA ran the level III fugacity model in EPISuite™ (U.S. EPA, 2012b) using emissions from a mass balance developed to account for the amount of TCE entering and leaving all facilities in the United States. For the mass balance EPA attempted to quantify the amount of trichloroethylene associated with each of its life cycle stages from introduction into commerce in the U.S. (from both domestic manufacture and import), processing, use, release, and disposal. The results of the modeling are presented in Appendix S. Discussion of assumptions and uncertainties

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	(U.S. EPA, 2018). This scenario estimates aqueous TCE concentrations that are 13,100% (131 times) above those estimated from TRI data. This would represent 6,812 pounds released to water by industrial uses. • Scenario 4 (problem formulation – High): Used to determine if using the higher 2016 DMR aqueous release estimates of 1,560 pounds (problem formulation 2.3.4 p. 34, last line) would lower the flux to water. Using this higher annual aqueous release (problem formulation 2.3.4 p. 34, last line) rather than the 52 pounds release (Table 2-7) produced an EPI Suite™ fugacity model output of 792% TCE increase in water over the concentration released to water. That represents 12,350 pounds of TCE released to water from industrial uses. So, a 30X increase in release to water only increases modeled surface water concentrations by 2X because the flux from other compartments is the dominant contributor to aqueous concentrations. • Scenarios 5 (Water Low + Air) and 6 (Water High + Air): Use the TCE releases to air and water from Scenarios 3 and 4 but assume that there is no release to surface soils and that there is no hydraulic connectivity from soils to surface water (both of which are not protective assumptions). Scenario 5 shows a 10,900% increase in TCE over the 52 pounds in Table 2-7, and Scenario 6 shows a 732% increase over the 1,560 pounds from 2016 DMR data, clearly demonstrating partitioning from air to water. One Committee member noted that overall, these EPI Suite™ fugacity outputs show that TCE releases to other abiotic media must be considered if aquatic receptors are to be protected. This fugacity evaluation also clearly demonstrates why EPA cannot pretend that discharges to non-aqueous media can be assessed separately. All biotic and abiotic compartments are interconnected through phase boundaries, and material transport across those boundaries does not behave as any policy or regulatory nexus dictates.	associated with TCE level III fugacity modeling and the SACC level III fugacity modeling results is presented in 2.1.3 Assumptions and Key Sources of Uncertainty for Fate and Transport.
SACC	**SACC COMMENTS:**	

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	Recommendation: Link monitoring data to upstream sources. • The Committee recommended that monitoring data must have some downstream hydraulic connection to the source. The Committee suggested that the simplest way to incorporate these data would be to identify which ones are indeed downstream with transit time of no more than 3 days and to situate another monitoring station downstream from the source, approximately 1/3 of the way (transit time) to the current monitoring station.	Release estimates and modeled concentrations in receiving water bodies are based on the scoped conditions of use, while monitoring data obtained from the WQP and/or peer-reviewed or grey literature sources are not. Therefore, there may or may not be a relevant proximity between the modeled surface water concentrations and the sampling sites with measured data obtained through systematic review.
Ethylene dichloride (EDC)/vinyl chloride monomer (VCM) facility releases are already regulated and should be separate COUs		
101	**PUBLIC COMMENTS:** EDC and VCM facilities have been regulated since 1994 under the Clean Air Act (CAA) by EPA's Hazardous Organics National Emission Standards for Hazardous Air Pollutants (NESHAP) rule, which established maximum achievable control technology standards to regulate the emissions of hazardous air pollutants (HAPs) from major source facilities. TCE is regulated as a HAP under section 112 of the CAA. Under this rule, emissions of HAPs at EDC/VCM facilities are highly controlled by this rule, including leak detection and repair requirements to prevent occupational exposure. As a result of this extensive regulation, all HAPs produced from this source category including TCE have been controlled and EPA must consider this a separate COU.	EPA agrees air releases from these facilities are regulated under NESHAPs, but TCE releases to water from these facilities is in scope for the risk evaluation as discussed in Section 1.4.2 of the risk evaluation.
Impact of pandemic		
81	**PUBLIC COMMENTS:** How will the global outbreak of COVID-19 affect TSCA and the percentage of TCE or any other toxic in drinking water?	Thank you for your question related to Coronavirus (COVID-19). Please refer to frequent questions to Coronavirus (COVID-19).

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3. Environmental Hazard

Environmental Hazard		
Charge Question 3.1: Please comment on EPA's approach for characterizing environmental hazard for each risk scenario (*e.g.,* acute aquatic, chronic aquatic). What other additional information, if any, should be considered (Section 3.1) **Charge Question 3.2:** Please comment on the use and interpretation of Species Sensitivity Distributions (SSDs) and hazardous concentrations (HC_{05}s) for ecological risk characterization and provide any specific suggestions or recommendations for how this information could inform EPA's risk assessment for TCE or other solvents (Section 3.1).		
#	**Summary of Comments for Specific Issues Related to Charge Question 3**	**EPA/OPPT Response**
Use/interpretation of SSDs and/or HC_{05} values for ecological risk characterization		
SACC	**SACC COMMENTS:** The Committee supports EPA's use of SSDs in the development of values intended to be protective of all aquatic receptors. It was encouraging that an SSD is used in conjunction with most sensitive species data for COC determinations. The inclusion of most sensitive species estimates of toxicity are warranted as often there is not enough sublethal endpoint data (*e.g.,* reproduction data) to support SSD calculations. Thus, the Committee considered a combination of both processes for development and further support of the COC as an appropriate exercise. • With one potential exception, values that were derived for acute and chronic exposures to aquatic organisms are reasonable, although there was not agreement on the magnitude of assessment factors (AFs) used; however, appropriate references are provided. It was also encouraging that sublethal endpoints of growth and reproduction were used to determine chronic values (ChV) for aquatic invertebrates.	EPA appreciates the support of SSDs and sublethal endpoints used in the Risk Evaluation and considered the modification of the assessment factors (AFs) used to derive COCs from the HC_{05}s (from the SSDs). In response to the SACC comments, EPA modified the AF for the algae SSD from 1 to 5 because EC_{50}s were used to derive the SSD rather than EC_{10}s or ChVs. EPA also modified the AF for the acute SSD from 1 to 5 to account for the small sample size used in the SSD, which encompassed multiple taxa.
SACC	**SACC COMMENTS:** Recommendation: Describe how the HC_{05} is computed and what it represents. It is unclear how to interpret an HC_{05} comprised of both EC_{50} and LC_{50} data. More description is needed on the methods used to derive those	EPA added the raw data used in each SSD and how it was decided to exclude any toxicity values from the SSD in Appendix E. EPA also added more explanation of what the HC_{05} represents in Section 3.1.3 in the Risk Evaluation.

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	values and how they would be valuable in advance. Section E1 only describes the tool used to compute the values, provides no additional justifications, and cites Etterson (2019), which does not provide a description of the methods used.	The SSD for algae used only EC_{50} values measuring growth, and the SSD for acute aquatic organisms used LC_{50}s for fish, amphibians, and invertebrates, and for invertebrates EC_{50}s measuring immobilization were also used because it is difficult to distinguish between death and immobilization for aquatic invertebrates. The above explanation was added to Section 3.1.3 of the Risk Evaluation.
SACC	**<u>SACC COMMENTS:</u>** • One Committee member suggested that the mantra that only toxic endpoints of mortality, growth, and reproduction are "populationally relevant" is fundamentally flawed. Since there is no direct knowledge regarding the criteria important in regulating the populations of any of the aquatic communities from where there are releases, it is improper to characterize any toxic endpoint necessarily of having "direct population level effects." Many populations are regulated by predator activity that makes narcosis or lethargy very important. In many natural systems, r-selected organisms (*i.e.,* ones that produce many eggs/individuals) lose a large proportion to events resulting in mortality or otherwise removing individuals from the population in pristine ecosystems. • The member recommended selecting endpoints by thinking in terms of any adverse effects that are potentially relevant to maintaining population size; such endpoints would include those such as lethargy (which is the result of narcosis and results in slow movement making individuals more susceptible to predation) and developmental affects that could ultimately result in mortality or otherwise removing individuals from of the reproduction pool. However, many of the described mechanistic effects could be characterized as endpoints of uncertain biological significance or those of an adaptive response, which would not fit this definition.	EPA used the best available science and reasonably available information during the data integration process, including effects on behavior and reproduction. The committee correctly notes that mechanistic data found in the studies for TCE could not be directly connected to an apical endpoint that would have an effect on population size. Therefore, EPA did not use them quantitatively to calculate Concentrations of Concern (COCs). However, the mechanistic data was described and used qualitatively.

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	• Two other Committee members mentioned that there are regulatory requirements associated with mortality, growth, and reproduction and recommended EPA consider those criteria when choosing endpoints.	
103	**PUBLIC COMMENTS:** EPA should clarify the importance of ecological risks to algae compared to all other aquatic species which were assessed and aggregated (*i.e.,* fish, amphibians, and aquatic invertebrates). It is unclear as to why algae represent a special case that should be evaluated independently.	Algae were assessed separately from other aquatic species, because algae tests and endpoints do not fit into the traditional definitions of acute and chronic durations. Algae was assessed separately and not incorporated into acute or chronic COCs, because durations normally considered acute for other species (*e.g.,* 48, 72 hours) can encompass several generations of algae.
47	**PUBLIC COMMENTS:** For purposes of environmental risk assessment, EPA selected and used a chemical concentration (HC_{05} = 52,000 ppb) as a hazard level that was extrapolated from the algal SSD by using a specified percentile of the distribution. We believe that it is inappropriate for EPA to override the more sensitive algal COC (3 ppb) by using the SSD projections in assessing risks. • EPA acknowledges that the algal SSD only includes EC_{50} values to compare between high- and medium-quality studies of nine species, and it does not capture some of the lowest reported toxicity values. We believe it would be more environmentally protective to include results from testing these more sensitive species. EPA specifically excludes lowest-observed-effect concentrations (LOECs) and no-observed-effect concentrations (NOECs), *e.g.,* the ChV of 0.03 mg/L for algal growth and metabolism derived from Labra et al. (2010). Given the great difference between the acute and chronic values and the need to protect the most sensitive species, it is very important to use only the algal COC of 3 ppb. • Does TSCA mandate protecting 95% of all species or 100% of all	EPA had more confidence in the probabilistic approach used to derive the COC from the SSDs, and the SACC generally agreed with EPA's approach for algae. The SACC suggested using a higher assessment factor, and EPA agreed. From draft to final version of the TCE Risk Evaluation EPA changed the assessment factor from 1 to 5 to account for the uncertainties around using EC_{50}s rather than ChVs. If sufficient ChVs had been available EPA would have used them instead of EC_{50}s. This change has been made in Section 3.1.5. TSCA does not mandate 95% of all species be protected; however, the 95% cutoff is a widely accepted cutoff accepted by jurisdictions around the world after extensive back and forth with scientists and policy makers (U.S. EPA, 1985).

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	species? Given the very wide range of separation (four orders of magnitude) between the algal COC (3 ppb) and the SSD-generated algal HC_{05} (52,000 ppb) for TCE, it is important to address the sensitivity of all algal species. Guiry (2012) conservatively estimated that there are 72,500 algal species, discounting diatoms whose numbers have been estimated to be over 200,000 species. TSCA obligates protection of the most sensitive species, and a more protective approach would be to use the 3 ppb COC, and to not use the statistically derived HC05 of 52,000 ppb. • For comparative purposes, approaches for setting ChVs for aquatic invertebrates and fish have traditionally made use of the maximum acceptable toxicant concentration (MATC) concept to help set water quality regulations for protecting aquatic life. MATCs are usually reported as geometric means between a NOECs and LOECs. Given the need to protect all algal species, and the very wide range between the algal EC_{50} and HC_{05} for the same species, it is critically important to firmly establish the COC at 3 ppb, and to not use the statistically derived HC_{05} of 52,000 ppb.	
103	**PUBLIC COMMENTS:** EPA does not state why it has chosen to take the SSD approach for the ecotoxicity data within the context of tiered environmental risk assessment. The TCE assessment appears to not conform to the general data structures (minimum numbers of taxa, SSD quality assessment, goodness-of-fit assessment, and other factors) to either Office of Water (OW) or Office of Pesticide Programs (OPP) practices. EPA should consider developing guidance specific to OPPT for use of SSD and also should consider adding a flow chart to indicate when an SSD is necessary for risk evaluation purposes under TSCA. Specific recommendations on SSD include: • EPA should provide greater transparency regarding its tiered environmental risk assessment process and the decision to evaluate the algae ecotoxicity data separately using the SSD approach. EPA should clarify its tiered environmental risk assessment process and	EPA had more confidence, given the weight of the scientific evidence, in the probabilistic approach used to derive the COC from the SSDs, and the SACC generally agreed with EPA's approach. The SACC suggested using a higher assessment factor for the COCs derived from the HC_{05}s, and EPA agreed. From draft to final version of the TCE Risk Evaluation EPA changed the assessment factor from 1 to 5 to account for the uncertainties around using EC_{50}s rather than ChVs. If sufficient ChVs had been reasonably available, EPA would have used them instead of EC_{50}s. The AF change has been made in Section 3.1.5.

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	the place the SSD occupies in tiered ecological hazard assessment, including how an SSD is fit-for-purpose in this instance. • EPA should articulate and apply best practices in developing an SSD. Several recent peer-reviewed articles are available that describe these practices, including Belanger et al. (2017), Carr and Belanger (2019), and Belanger and Carr (2019). • EPA should clarify whether its COC in practice will be derived from the lowest single chronic inhibition value from among the algal studies or the HC5 based on acute inhibition. As these are 3+ orders of magnitude apart, the choice and assumptions applied are critical. • It does not appear that the public has access to EPA's SSD calculator algorithms (Etterson et al., 2019). In order to allow for recreation of the SSD estimates using other software available to the public, it would be helpful to have an actual table of input values that EPA used. This would give a firmer assessment of model choice and the quality of the SSD output.	OPPT consulted with other offices within the EPA including OW, OPP, and ORD as it used SSDs under TSCA. OPPT is in the process of developing an SOP for using SSDs in TSCA Risk Evaluations. EPA added more explanation to the TCE Risk Evaluation in Section 3.1.3 and 3.1.4. EPA has since made the SSD algorithms publicly available on HERO: (Etterson, 2020).
50	**PUBLIC COMMENTS:** EPA evaluated the algal ecotoxicity data and acute ecotoxicity data using the SSD approach. The SACC should evaluate and comment on the appropriateness of using the SSD approach on ecotoxicity data and the details of EPA's application of the approach.	The SACC was in support of using the SSD and asked for more transparency in what data was used in the SSD and more explanation about what the results of the SSD mean. Both were added to Section 3.1.3, 3.1.4, and Appendix E of the Risk Evaluation.
56, 108	**PUBLIC COMMENTS:** EPA's analysis may have underestimated the risk from these releases especially for algae. EPA justifies its calculated COC as being representative for algae species "as a whole." EPA determined that "as a whole" in this case constitutes nine species of algae. Yet algae are an incredibly diverse (and poorly defined) group of organisms that represent 15 phyla and 54 classes; estimates of total species of algae are between 72,000 and 1 million. To conclude that a COC of 52 mg/L is protective of algae "as a whole," based on only nine species, with a concentration that is over 17,000 times higher than the COC EPA	EPA had more confidence, given the weight of the scientific evidence, in the probabilistic approach used to derive the COC from the SSDs, and the SACC generally agreed with EPA's approach for algae. The SACC suggested using a higher assessment factor, and EPA agreed. From draft to final version of the TCE Risk Evaluation EPA changed the assessment factor from 1 to 5 to account for the uncertainties around using EC50s

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	derived for the most sensitive species of algae identified for the draft risk evaluation is indefensible. Instead, EPA should use the most sensitive species as its indicator organism to develop appropriately protective COCs. • Using the far more appropriate COC of 3 ppb, EPA identified risks from exposure to TCE to the most sensitive algae specie at 521 facilities (p. 354); nevertheless, EPA dismissed these risk quotients (RQs) as actually showing no risk for "algae species as a whole" based on its questionably calculated COC (pp. 378-379).	rather than ChVs. If sufficient ChVs had been reasonably available EPA would have used them instead of EC_{50}s. This change has been made in Section 3.1.5.
47	**PUBLIC COMMENTS:** • EPA used algal data for nine species to produce an SSD, which was then used to calculate an HC_{05} of 52 mg/L (or 52,000 ppb). This HC_{05} estimates a concentration that EPA maintains is hazardous for 5% of species. EPA maintains that HC_{05} can also be used, in addition to the algal COC, to estimate the concentration of TCE that is expected to protect 95% of algae species. We would ask EPA to provide further explanation for the basis and methods for extrapolating from COC-based adequate-quality results of testing nine species to protecting 95% of all of the approximately 72,500 algal species, *i.e.,* 0.95 x 72,500 algal species = 68,875 species. • Table 4-1 in the draft risk evaluation indicates at least 30 instances where RQs ≥1 appear to have been met or exceeded, indicating potential risks to the aquatic environment. EPA used algal SSD to argue that these were not appreciable risks to most algal species and that algal species as a whole were not a problem for aquatic environmental risk. We disagree with this finding because the algal SSD works to diminish protection for the more sensitive algal species. These RQs clearly indicate a potential risk to aquatic algae. • The commenter highlighted several examples from Table 4-1 where RQs >1 were exceeded under the TCE use categories of processing reactant, in repackaging, open-top vapor degreasing, adhesives, sealants, paints and coatings, other industrial uses, industrial processing aid, other commercial uses, and process solvent	EPA had more confidence, based on the weight of the scientific evidence, in the probabilistic approach used to derive the COC from the SSDs than the deterministic approach, and the SACC generally agreed with EPA's approach for algae. The SACC suggested using a higher assessment factor for the COC derived from the HC_{05} due to the fact that less than 20 species were used to create the SSD. EPA agreed to make the change. From draft to final version of the TCE Risk Evaluation EPA changed the assessment factor from 1 to 5 to account for the uncertainties around using EC50s rather than ChVs. If sufficient ChVs had been reasonably available EPA would have used them instead of EC_{50}s. This change has been made in Section 3.1.5.

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	recycling and worker handling of wastes, thereby underscoring EPA's inappropriate approach to assessing risks to algae.	
47	**PUBLIC COMMENTS:** There is agreement that the New Rochelle STP appears to present little or no risk to aquatic algal species.	Thank you for your comment.
Alternative use/interpretation of SSDs or HC_{05} values is suggested		
SACC	**SACC COMMENTS:** Recommendations: (1) Use EC_{50} or EC_{20} values in computing the SSD. (2) If computing an SSD is not possible, use the EC_{20} of the most sensitive species as the point of departure (POD). • The SSDs are a good visualization tool for determining the potential relative impact to different species and may inform actions depending on the dynamics of TCE in an aquatic environment. However, for TCE, given data gaps for the development of the curves, one Committee member asserted that no definitive conclusions can be made for algae. In addition, one limitation of SSDs is that outputs do not include the lowest toxicity values reported (including LOECs and NOECs). Adding the values may provide additional visualization of the data that may help in supporting COC derivation. • The Committee recommended that SSDs be developed using EC_{50} (or optimally EC_{20}) values exclusively to develop a sublethal value that is expected to be protective for 95% of the species. If sufficient data are not available for an SSD derivation, then the use of the EC_{20} for the most sensitive species as a POD from which to apply an AF to derive a COC is reasonable. • Aqueous concentrations should be consistently expressed as µg/L or mg/L in the main text, to avoid confusion. In fact, the information in Appendix E shows the average of HC_{05} is 9,900 µg/L and a safety factor of 5 places that value at 1,959 µg/L. To further illustrate this, Figure Apx E7 shows three closely agreeing fits for HC_{05} and one outlier. Thus, the acute COC should exclude the Gumbel fit and thus	For the chronic COC EPA did use the EC_{20} as the most sensitive point of departure. For the algae COC, EPA used EC_{50}s measuring growth to create the SSD, and for the acute COC EPA used LC_{50}s for consistency across taxa to create the SSD. The SACC suggested using a higher assessment factor for the COCs derived from the HC_{05}s from the acute SSD and the algae SSD. EPA agreed to make the change. From draft to final version of the TCE Risk Evaluation EPA changed the assessment factor from 1 to 5 to account for the uncertainties around using LC50s/EC50s rather than ChVs and to account for the number of species used in each SSD being smaller than 20. This change has been made in Section 3.1.5.

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	the HC_{05} would be ~6.3 mg/L or 6,300 µg/L. A safety factor for not having over 20 species (*i.e.,* the SSD computation is extrapolating beyond the range of the data) would then provide a concentration that is lower than currently estimated by EPA.	
COC derivation		
SACC	**SACC COMMENTS:** While a fish 32-day growth value is used for COC determination (7.88 mg/L), it is unclear why the lower 4 mg/L tadpole survival NOEC is neglected. Since the values are on the same order of magnitude, it does not appear to affect overall COC estimates.	To assess aquatic toxicity from chronic exposures, data for three taxonomic groups were described in the acceptable literature: fish, amphibians, and aquatic invertebrates. However, for amphibians, only a NOEC was established. Therefore, the endpoints for fish and aquatic invertebrates (ChVs, an EC_{20}, and an EC_{50}) were more biologically relevant, because they measured a toxic effect, whereas the NOEC did not. Of the more relevant values, the most sensitive was the EC_{20} measuring growth in fish at 7.88 mg/L. The EC_{20} was from a high-quality study, whereas the NOEC of 4 mg/L was from a medium quality study. Considering both the relevance and the quality, EPA had more confidence in the EC_{20} for fish than in the NOEC for tadpoles. Additional explanation was added to the Risk Evaluation in Section 3.1.4 Weight of the Scientific Evidence.
SACC	**SACC COMMENTS:** It is typically inappropriate to treat median lethal and median sub-lethal values equally (draft risk evaluation, p. 198). However, if the mode of action (MOA) or endpoints are consistent with those that could reasonably be assumed to result in mortality (*e.g.,* narcosis, terata), values would largely be equivalent, and hence appropriate, to treat equally. The draft risk evaluation needs to specify the endpoints for the EC_{50} values used. If not, use the lowest biologically relevant endpoint	The SSD for algae used only EC_{50} values measuring growth, and the SSD for acute aquatic organisms used LC_{50}s for fish, amphibians, and invertebrates, and for invertebrates EC_{50}s measuring immobilization were also used because it is difficult to distinguish between death and immobilization for aquatic invertebrates. The

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	value and apply an AF, then carry this value through the risk assessment.	above explanation was added to Section 3.1.3 of the Risk Evaluation.
SACC	**SACC COMMENTS:** Recommendation: Justify the use of the geometric mean in calculating lethal and nonlethal acute effects for invertebrates. • That the geometric mean is used to calculate a COC from both lethal and non-lethal data for acute invertebrate effects also requires further justification. What justifies the mean value when endpoints are different? Are all studies otherwise equivalent (see previous comment)? What data justify the geometric and not the arithmetic mean? Precisely, why is the HC_{05} not used as a POD for acute exposures to aquatic invertebrates (9.9 mg/L)?	For invertebrates LC_{50}s and EC_{50}s measuring immobilization were used, because it is difficult to distinguish between death and immobilization for aquatic invertebrates. A mention of this was added to Section 3.1.3 of the Risk Evaluation. EPA derived the geometric mean, because the hazard values for all three species were similar, and because EPA had more confidence in a COC derived from a geometric mean for three species than a COC derived from one value from one species. EPA added a justification for using the geometric mean in calculating an acute COC in the 3.1.5 Section of the Risk Evaluation.
SACC	**SACC COMMENTS:** Recommendation: Distinguish between study quality and study relevance in weight-of-evidence (WOE) considerations. • There is a difference between data quality and data relevance (see p. 197, lines 287-315). Some very high quality toxicity data are not relevant to derive toxicity values from (*e.g.,* mechanistic, *in vitro* data, population data, lack of dose response); however, they still have utility in addressing questions regarding biological plausibility and addressing issues associated with extrapolation of effects across species and populations. • The Committee recommended that EPA make this distinction between quality and relevance in judging total WOE in the development of toxicity reference values. Here, data relevance would directly refer to dose response information that could be used to develop a POD or COC.	The difference between quality and relevance is outlined in Section 3.1.4 Weight of the Scientific Evidence. EPA did consider both quality and relevance separately and added detail to Section 3.1.4 about studies used to derive the COCs to more clearly explain the thought process that went into deciding which toxicity values to use.
SACC	**SACC COMMENTS:**	

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	Recommendation: Consider taxonomic representativeness of data and MOA information in setting AFs. • Several Committee members found that the use of AFs of 10 and 5 to adjust the PODs for chronic and acute COCs appropriate and consistent with the scientific literature that have evaluated sensitivities of aquatic organisms using SSDs and NOECs; however, it is stressed that NOECs are often artifacts of study design and recommended that EPA consider taxonomic representativeness of the data and any available MOA or mechanistic data when deciding on the magnitude of AFs (see Belanger and Carr, 2019). • One Committee member proposed that the lack of an aquatic vertebrate reproduction endpoint may suggest an uncertainty factor (UF) of 100 rather than 10 be used; however, if retained, the sensitivity of algae seems to allow conservatism in other COC calculations (Keinzler et al., 2017). The lack of reproductive data should also be discussed as an uncertainty.	EPA is in the process of evaluating the body of reasonably available literature in order to determine whether to revise standards for application of AFs and acute to chronic ratios for the next 20 high-priority substances undergoing risk evaluation. EPA considered the (Kienzler, 2017) study in its assessment for the final Risk Evaluation. Until the body of scientific evidence for assessment factors is evaluated, EPA will continue to use OPPT methodology as cited in the risk evaluation (U.S. EPA, 2013, 2012) and apply an AF of 5 for acute and 10 for chronic aquatic invertebrate data. EPA considers these AFs to be protective of aquatic invertebrates from acute and chronic exposures to neutral organic substances such as TCE, which produce toxicity from simple narcosis.
SACC	**SACC COMMENTS:** Recommendation: Summarize environmental hazard conclusions in a table. An example table was provided.	EPA added the suggested summary table to Section 3.1.7.
103	**PUBLIC COMMENTS:** EPA should provide more detail in the ecological hazard assessment section, specifically addressing the impact of the multiple concentrations of concern that were calculated, the data quality of key algal study, and the application of SSD. • EPA should consider providing a flow chart to describe the tiered approach to ecological hazard assessment to better explain when the application of advanced tools, such as SSD, is necessary	EPA added information in multiple subsections in Section 3 and in Appendix E to explain the toxicity data that went into the COCs, and the decisions that were made to use the SSD over the deterministic approach for calculating COCs.
103, 50	**PUBLIC COMMENTS:** EPA should clarify the purpose of each of the COCs and indicate which, if any, is most important for understanding whether an unreasonable risk might occur.	EPA added information in multiple subsections in Section 3 and in Appendix E to explain the toxicity data that went into the COCs, and the

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	• EPA derived an acute COC, a chronic COC (with algal ecotoxicity data excluded), an algal COC (using only algal ecotoxicity data), and an algal HC_{05} using the SSD approach. The importance of each of these is unclear and certainly the extreme divergence between the algal COC and algal HC_{05} (four orders of magnitude) is confusing. The SACC should comment on EPA's approach and the appropriateness and relevance of each of these thresholds.	decisions that were made to use the SSD over the deterministic approach for calculating COCs. Additionally, EPA added a summary table to Section 3.1.7 with a description of each COC, and what toxicity data and AF was used to calculate it.
47	**PUBLIC COMMENTS:** EPA calculated the COCs for aquatic species using geometric means and statistical modeling of toxicity values for multiple species. Instead, EPA should have used both acute and chronic toxicity values for the most sensitive species within each major taxonomic group (*e.g.,* algae, aquatic invertebrates, and fish). • TSCA clearly requires EPA to protect all exposed aquatic, benthic, and terrestrial species against adverse effects from exposure to industrial chemicals. Modeling chemical toxicity is useful to investigate groupings and trends in toxicity data and, where no data exist, to generate toxicity data using structure-activity relationships. Nevertheless, valid testing results are always preferable to results of modeling, particularly where the models work to reduce apparent toxicity, *e.g.,* by using averaged results of individual studies in place of results from studies of the most sensitive species, and, consequently, minimizing levels of concern for adverse effects to the natural environment.	EPA weighed the scientific evidence and during data integration considered the reasonably available data to calculate the COCs with the highest quality and relevant data. EPA generally prefers probabilistic approaches (*e.g.,* SSDs) to data integration than deterministic ones (*e.g.,* using just the most sensitive value, or a geometric mean of several values).
Consideration of Labra et al. (2010) study in COC derivation		
SACC	**SACC COMMENTS:** Recommendation: Discuss reasons for the 4-fold difference in acute algal COC estimates based on the EC_{20} versus the SSD HC_{05} values. • The draft risk evaluation computes two COCs for acute algal effects, one using the EC_{20} for the most sensitive species and one using the SSD HC_{05} value. These values vary by more than four orders of magnitude, yet no explanation is provided for why this might be reasonable. When values differ by such a large extent, further	TCE had a robust dataset for algae in the reasonably available literature. The data show that there is a wide range in toxicity values for algae exposed to TCE, likely because of species to species variation but also because of lab to lab variation. Additionally, the Labra value was derived from NOEC and LOEC values rather

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	investigation is warranted. There could be study quality issues or simply false positive outcomes that may help explain these results. Was this study repeated? • The Committee recommended a more robust assessment of the Labra et al. (2010) study to evaluate its potential as outlier data and further justify the use of these data over the HC_{05} designed to protect 95% of the species. Further, it is not clear why the Labra et al. (2010) quality metric is downgraded to medium while most individual quality components are rated high.	than the EC_{50}s that were used in the SSD. Unfortunately, the same species from the Labra study did not have an EC50 available in the literature for comparison. Labra et al. (2010) was not downgraded to a medium. The first draft of the supplemental file looked as though it was downgraded, but the quality score it received should have categorized it as a medium. This was corrected in the final version of the supplemental file for environmental hazard data quality evaluation.
103	**PUBLIC COMMENTS:** The key algal study by Labra et al. (2010) should be viewed as an outlier. *Raphidocelis* is nearly always equivalent in sensitivity to *Desmodesmus subspicatus*. According to Brill et al. (2016), one would expect these taxa to be within a factor of 2 of each other, yet for TCE, they are about 50-fold different. The variance estimates of the algal cell density data are incredibly small, while a coefficient of variation (CV) of 5-15% is expected. The inoculum density to terminal cell density should be at least 16-fold and for this species, more like 100-fold, where in this case, it is about 8-fold and would not meet standard test validity criteria. Moreover, the general acute:chronic ratio for algae is typically in the realm of 3-5; in large data reviews, it is about 4.35. • EPA should more closely review the data from Labra et al. (2010) and determine whether it is appropriate for inclusion within the environmental hazard data set.	Labra et al. (2010) was evaluated for quality and given a medium quality score. However, during data integration EPA was also able derive a COC using a probabilistic method using an SSD, which was preferred over the deterministic method using Labra et al. (2010). EPA has more confidence, based on the weight of the scientific evidence, and prefers using probabilistic methods over deterministic methods. Part of the reason EPA has confidence in and prefers the probabilistic method for calculating a COC is that it takes multiple studies and species into consideration instead of a single study and species, which reduces the effect that an outlier study may have on the COC.
47	**PUBLIC COMMENTS:** The paper (Labra et al., 2010) used to set the 3 ppb algal COC was evidently not used in developing the algal COC, and EPA explained that omission by pointing out that Labra et al. (2010) had data quality limitations, and that the SSD used only medium- or high-quality studies.	Labra et al. (2010) was evaluated for quality and given a medium quality score. However, during data integration EPA was also able derive a COC using a probabilistic method using an SSD, which

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	A more environmentally-protective approach would have been to include Labra et al. (2010) in developing the SSD because the effect levels for growth and metabolism (ca. 30 ppb) reported in Labra et al. (2010) were orders of magnitude below those used in the SSD. • While the algal testing results reported by Ando et al. (2003) were of considerably lower quality than Labra et al. (2010), they found effect levels (*Volvulina steinii* 10-day LOEC: 3 ppb) that were more sensitive by a factor of 10 than those Labra et al. (2010) reported. Acknowledging the weaknesses found in both the Labra et al. (2010) and Ando et al. (2003) studies, they demonstrate the existence of effects to different algal species occurring at concentrations that are orders of magnitude lower than those used in EPA's algal SSD. This argues for the importance of not diminishing the merits of results from testing more sensitive species. • Also, data from Labra et al. (2010) resulted in a ChV (3 ppb) used in EPA's TCE report. Had the Ando et al. (2003) study been more rigorous, it would have resulted in a ChV of 0.3 ppb. The SSD resulted in an HC_{10} of 52,000 ppb based on toxicity testing designed with relatively short durations (typically 96 or fewer hours) compared to the 10-day duration reported by Ando et al. (2003). While their results were not used quantitatively during data integration, they are useful in pointing out the need for not diminishing the 3 ppb COC based on Labra et al. (2010). This is because the data demonstrate that algal effects at unusually low TCE concentrations to different species are real and should be incorporated in, not diminished by, SSD analyses in EPA's TCE risk evaluation and would be more protective of the natural environment.	was preferred over the deterministic method using Labra et al. (2010). EPA has more confidence, based on the weight of the scientific evidence, and prefers using probabilistic methods over deterministic methods. Part of the reason EPA has confidence in and prefers the probabilistic method for calculating a COC is that it takes multiple studies and species into consideration instead of a single study and species, which reduces the effect that an outlier study may have on the COC.

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4. Occupational and Consumer Exposure

Occupational and Consumer Exposure
Charge Question 4.1: Please comment on the approaches and estimation methods, models, and data used in the occupational exposure assessment (Section 2.3.1). **Charge Question 4.2:** Please provide any specific suggestions or recommendations for alternative data (modeling or monitoring) or estimation methods that could be considered by the Agency for conducting the occupational exposure assessment. If so, please provide specific literature, reports, or data that would help us refine the exposure assessment (Section 2.3.1). **Charge Question 4.3:** Please comment on assumptions used in the absence of specific exposure information (*e.g.,* dermal surface area assumptions: [high-end values, which represents two full hands in contact with a liquid: 890 cm^2 (mean for females), 1070 cm^2 (mean for males)] and [central tendency values, which is half of two full hands (equivalent to one full hand) in contact with a liquid and represents only the palm-side of both hands exposed to a liquid: 445 cm^2 (females), 535 cm^2 (males)]). Please also consider these values in the context of different lifestages and body weights (Section 2.3.1.2). **Charge Question 4.4:** Please comment on EPA's approach to characterizing the strengths, limitations and overall confidence for each occupational exposure scenarios presented in Section 2.3.1. Please comment on the appropriateness of these confidence ratings for each scenario. Please also comment on EPAs approach to characterizing the uncertainties summarized in Section 2.3.1.3. **Charge Question 4.5:** Please comment on the adequacy, appropriateness, and transparency of EPA's approach and the assumptions EPA used to characterize ONU exposure via this approach (Section 2.3.1). **Charge Question 4.6:** Are there other approaches or methods for assessing ONU exposure for the specific condition of use (Section 2.3.1)? **Charge Question 4.7:** Please comment on the appropriateness of the approaches, models, exposure or use information and overall characterization of consumer inhalation and dermal exposures for users and bystanders for each of the identified conditions of use. What other additional information, or approaches, if any, should be considered (Section 2.3.2)? **Charge Question 4.8:** Please recommend any additional data sources or studies that may be more reflective of current consumer use patterns for specific conditions of use (Section 2.3.2). **Charge Question 4.9:** Dermal exposure was evaluated using the permeability sub-model (P_DER2b) within CEM Version 2.1. Please comment on the suitability and use of this modeling approach for this evaluation. Please provide any suggestions or recommendations for alternative approaches, dermal methods, models or other information which may guide EPA in developing and refining the dermal exposure estimates (Section 2.3.2.4.1). **Charge Question 4.10:** Please comment on EPA's approach to characterizing the strengths, limitations and overall confidence for each consumer exposure scenario presented in Section 2.3.2. Please comment on the appropriateness of the confidence ratings for each scenario. Please also comment on EPA's approach for characterizing the uncertainties summarized in Section 2.3.2.7.

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#	Summary of Comments for Specific Issues Related to Charge Question 4	EPA/OPPT Response
EPA's exclusion of exposure to the general population is invalid		
49, 56, 65, 74, 86, 90, 99, 104, 108	**PUBLIC COMMENTS:** EPA abdicated its responsibility under TSCA to identify and evaluate risks to the general population by excluding release of TCE to indoor and outdoor air, water, and land, or to consider exposure to background levels. The most recent TRI data for TCE establishes that TCE is released to air, water, and land in significant quantities. • Each of these pathways is alone responsible for cancer and non-cancer risks to large segments of the population that exceed EPA benchmarks. • There is a potential for underestimating consumer inhalation exposures, particularly for populations living near a facility emitting TCE or living in a home with other sources of TCE, such as TCE-containing products in the home. • EPA asserted that exposures to the general population are "adequately managed" without providing scientific rationale for the assumption or analysis of the standards under the other statutes, which may not be strictly health based. Unlike TSCA, other statutes consider factors such as cost and feasibility when setting standards. • TSCA empowers EPA to look at the risk posed by the chemical broadly without focusing on source-specific technology, costs of regulation, or what standards are "achievable" for each source category. EPA must evaluate a chemical's risk "without consideration of costs or other non-risk factors." TSCA requires EPA to consider the "COU" of a chemical, with no distinction drawn between stationary sources and other sources, and focuses on the risks posed by chemical substances and EPA actions that can ameliorate those risks, without considering "standards of performance." • First, the updated law specifies that, "the Administrator shall consider and publish a statement based on reasonably available	During Problem Formulation, EPA acknowledged that general population exposures may occur through air, water, and land/soil pathways. However, in the Risk Evaluation, EPA did not include pathways under programs of other environmental statutes, administered by EPA. Because stationary source releases of TCE to ambient air are covered under the CAA, EPA did not evaluate emission pathways to ambient air from commercial and industrial stationary sources or associated inhalation exposure of the general population. Because the drinking water exposure pathway for TCE is covered in the SDWA regulatory analytical process for public water systems, EPA did not include this pathway in the risk evaluation for TCE under TSCA. In Problem Formulation, EPA also found general population exposures to TCE via underground injection, RCRA Subtitle C hazardous waste landfills, RCRA Subtitle D municipal solid waste (MSW) landfills, and on-site releases to land from industrial non-hazardous waste and construction/demolition waste landfills are under the jurisdiction of and addressed by other EPA-administered statutes and associated regulatory programs. EPA did not include Superfund on-site releases to the environment, as they are under the jurisdiction of CERCLA. Lastly, EPA did not include emissions to ambient air from

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	information with respect to (i) the effects of the chemical substance or mixture on health and the magnitude of the exposure of human beings to the chemical substance or mixture…" This requirement is chemical-specific and is not conditioned on specific COU. • EPA can only rely on statutory authorities other than TSCA in compliance with TSCA Section 9 (notably, the TSCA Section 9 process occurs *after* EPA has completed a comprehensive risk evaluation finding unreasonable risk). • EPA should conduct sensitivity analyses to quantify the potential extent of underestimation due to excluding these background exposures. • Ignoring exposures subject to non-TSCA regulation will likely delay protection to U.S. residents, as it is not likely that a TSCA evaluation will immediately trigger a regulatory review by other EPA programs. • EPA must justify this decision or quantify the number of people expected to experience substantial exposures to background concentrations of TCE. • Congress expressly chose to separate risk evaluation and risk management into different procedural steps (with risk evaluation preceding risk management) to ensure that EPA provided a robust risk evaluation uncolored by non-risk factors or other risk management concerns. • The draft risk evaluation failed to provide missing analysis to support the conclusion that there is no unreasonable risk from certain exposures or combinations of exposures. • In order to decline an exposure pathway, EPA must first assess the level of exposure from the pathway individually and then consider how it combines with other sources of exposure.	municipal and industrial waste incineration and energy recovery units in the risk evaluation, as they are regulated under section 129 of the Clean Air Act. As explained in more detail in Section 1.4.2 of the Final Risk Evaluation, EPA believes it is both reasonable and prudent to tailor TSCA Risk Evaluations when other EPA offices have expertise and experience to address specific environmental media, rather than attempt to evaluate and regulate potential exposures and risks from those media under TSCA. EPA believes that coordinated action on exposure pathways and risks addressed by other EPA-administered statutes and regulatory programs is consistent with statutory text and legislative history, particularly as they pertain to TSCA's function as a "gap-filling" statute, and also furthers EPA aims to efficiently use Agency resources, avoid duplicating efforts taken pursuant to other Agency programs, and meet the statutory deadline for completing Risk Evaluations. EPA has therefore tailored the scope of the Risk Evaluation for TCE using authorities in TSCA Sections 6(b) and 9(b)(1).
56, 74, 90, 108	**PUBLIC COMMENTS:** Exclusion of general population exposure violates intent of the Lautenberg Act's and are contrary to the core mission of EPA to protect public health. Major exposure pathways are ignored. EPA, Centers for	

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	Disease Control and Prevention (CDC)/Agency for Toxic Substances and Disease Registry (ATSDR), and most states have documented TCE concentrations in ambient air, with elevated levels around sources and in highly populated areas. Exclusion of pathways of exposure from the risk evaluation is the definition of arbitrary and capricious conduct and a violation of TSCA. • TCE is pervasive in indoor air at concentrations documented to be several times higher than outdoor levels due to consumer products, vapor intrusion from subsurface contamination, and volatilization from contaminated drinking water. • CDC/ATSR has reported that TCE is the most frequently detected chemical contaminant in groundwater. • TCE has been found in a wide variety of foods. TCE has been detected in breast milk in the general population. Formula fed infants are also vulnerable because of the pervasive contamination of drinking water and their high ingestion rate. • Little or no explanation was provided for the decision to not to further analyze specific exposure pathways or receptors.	
90	**PUBLIC COMMENTS:** The general population and specifically low income and minority populations that are entitled to enhanced protection under Executive Order 12898 on Environmental Justice have been shown to be overburdened by community sources of TCE. ATSDR in its 2019 updated toxicologic profile on TCE notes that the most important routes of TCE exposure to the general public are through ambient air and the ingestion of drinking water. • Environmental Justice have been shown to be overburdened by community sources of TCE. It is the responsibility under TSCA to combine and assess various sources to the general population and in particular to vulnerable segments of the population.	EPA acknowledges low socioeconomic status as a susceptibility factor for PESS groups in Section 3.2.5.2. EPA uses the 99th percentile output of the PBPK model in order to account for the most toxicokinetically sensitive proportion of the population. See Sections 2.3.3, 3.2.5.2, and 4.4.1 in the risk evaluation for further discussions of PESS. TSCA § 6(b)(4)(A) requires that EPA conduct a risk evaluation to "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of cost or other non-risk

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		factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator, under the conditions of use." TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." EPA believes that the statutory directive to consider potentially exposed or susceptible subpopulations (PESS) and the statutory definition of PESS inherently include environmental justice populations. Thus, EPA's consideration of PESS in this risk evaluation addresses the requirements of the Executive Order. EPA seeks to achieve the fair treatment and meaningful involvement of any group, including minority and/or low-income populations, in the development, implementation, and enforcement of environmental laws, regulations, and policies. To this end, the Agency has already sought input from specific populations and public health experts in implementing TSCA and will continue to do so. EPA will also consider environmental justice populations in accordance

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		with the Executive Order as it develops risk management actions based on final TSCA section 6(b) risk evaluations.
56, 108	**PUBLIC COMMENTS:** EPA has ignored "take home exposures" whereby the family of a worker, including children, may be exposed via contact with the worker's contaminated clothing or skin.	The frequency and magnitude of take-home exposure is dependent on several factors, including personal hygiene and visibility of the chemical on skin or clothing. EPA does not have methods to reliably predict take-home exposure consistent with the mandate under TSCA section 26(h) to use the best available science.
SACC	**SACC COMMENTS:** Recommendation: Use other TCE exposure sources (*e.g.,* drinking water from wells, and other contributors to indoor concentrations) in addition to those from TCE-containing products to characterize consumer risks. One Committee member suggested that the draft risk evaluation could better characterize consumer risks by using an upper percentile of the residential exposures reported in the general population studies cited in the draft risk evaluation.	EPA did not consider background exposure that workers and consumers using products containing TCE might be exposed to in addition to exposures from conditions of use in the scope of the risk evaluation. This may result in an underestimation of risk, and additional discussion of this underestimation is found in Sections 2.3.2.6.1 and 4.4.2.
49, 99	**PUBLIC COMMENTS:** There is considerable evidence of TCE's ubiquitous presence in air, soil, and drinking water at levels that likely harm human health and contribute to ozone depletion and climate change. These exposure pathways cannot be ignored.	
EPA justification for excluding exposure pathways is not valid (general comments); EPA must assess total exposure		
104, 49	**PUBLIC COMMENTS:** In order to have a complete picture of how TCE endangers human health and the environment, all exposure pathways need to be considered and EPA should revise the draft risk evaluation of TCE to account for all sources of exposure including all reasonably foreseen COU.	The conceptual models only included exposure pathways that are within the scope of the risk evaluation. The environmental exposure pathways covered under the jurisdiction of other EPA-administered statutes and regulatory programs are not within the scope of the risk evaluation. As explained in more detail in

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		Section 1.4.2 of the Final Risk Evaluation, EPA believes it is both reasonable and prudent to tailor TSCA Risk Evaluations when other EPA offices have expertise and experience to address specific environmental media, rather than attempt to evaluate and regulate potential exposures and risks from those media under TSCA. EPA believes that coordinated action on exposure pathways and risks addressed by other EPA-administered statutes and regulatory programs is consistent with statutory text and legislative history, particularly as they pertain to TSCA's function as a "gap-filling" statute, and also furthers EPA aims to efficiently use Agency resources, avoid duplicating efforts taken pursuant to other Agency programs, and meet the statutory deadline for completing Risk Evaluations. EPA has therefore tailored the scope of the Risk Evaluation for TCE using authorities in TSCA Sections 6(b) and 9(b)(1).
108, 49, 99, 104, 88	**PUBLIC COMMENTS:** The exclusion of background exposures that workers and consumers experience through air, water, and other pathways undermines EPA's analysis of circumstances that EPA does analyze in the draft risk evaluation because it is the total level of exposure to a chemical that determines risk, and this includes exposures that are not generally attributable to any one use or source. • Congress wanted EPA to examine the combined impact of all sources and pathways of exposure and provided no exemption for environmental releases that might be subject to other environmental laws. • Other laws are not adequately addressing the contribution of air, soil, and drinking water to total risk. If these pathways are ignored, the	EPA did not consider background exposure that workers and consumers using products containing TCE might be exposed to in addition to exposures from conditions of use in the scope of the risk evaluation. This may result in an underestimation of risk, and additional discussion of this underestimation is found in Sections 2.3.2.6.1 and 4.4.2. EPA did not consider background exposure for workers, ONUs, consumers, and bystanders using products containing TCE who might be

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	result will likely be an incomplete understanding of TCE's risks and inadequate protection of health and the environment and for subpopulations with higher background TCE exposure levels. • EPA's decision to ignore exposures one-by-one rather than look at combined exposure is inherently inaccurate and will invariably lead to an underestimation of exposure and risk. EPA should revise the draft TCE risk evaluation so it accounts for all sources of exposure and risk and provides a complete understanding of how TCE endangers public health.	exposed to in addition to exposures from other conditions of use in the scope of the risk evaluation. This may result in an underestimation of risk, and additional discussion of this underestimation is found in Sections 2.3.2.6.1 and 4.4.2.
108	**PUBLIC COMMENTS:** For numerous sources of exposure, EPA treats the overall exposure from a particular pathway as "zero" or non-existent despite the fact that the available evidence that exposure occurs at levels well above zero. Humans and the environment are experiencing levels of exposure that EPA is willfully ignoring. • The draft risk evaluation does not establish that the regulation of these chemical substances under other statutes will eliminate exposures, and in fact establishes that exposures continue to occur in the real-world despite these statutes. • TSCA does not authorize EPA to ignore exposures because of other statutory authorities; EPA has to analyze all exposures. • EPA may only rely on actions under another statute if those actions will reduce an identified risk "to the extent necessary so that [it] no longer presents [an unreasonable risk of injury to health or the environment]." EPA cannot assume that other statutes, with different standards, meet TSCA requirements. • EPA makes no showing that its actions under other statutes reduce the risk "to the extent necessary so that [it] no longer presents [an unreasonable risk of injury to health or the environment]," and EPA does not present any actual analysis of "all relevant aspects of the risk" arising from the ignored exposures. EPA has undisputedly failed to comply with TSCA.	During Problem Formulation, EPA acknowledged that general population exposures may occur through inhalation, oral, and dermal. However, in the Risk Evaluation EPA did not include pathways under programs of other environmental statutes, administered by EPA. Because stationary source releases of TCE to ambient air are covered under the CAA, EPA did not evaluate emission pathways to ambient air from commercial and industrial stationary sources or associated inhalation exposure of the general population. Because the drinking water exposure pathway for TCE is covered in the SDWA regulatory analytical process for public water systems, EPA did not include this pathway in the risk evaluation for TCE under TSCA. In Problem Formulation, EPA also found general population exposures to TCE via underground injection, RCRA Subtitle C hazardous waste landfills, RCRA Subtitle D municipal solid waste (MSW) landfills, and on-site releases to land from industrial non-hazardous waste and construction/demolition waste landfills are under

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		the jurisdiction of and addressed by other EPA-administered statutes and associated regulatory programs. EPA did not include Superfund on-site releases to the environment, as they are under the jurisdiction of CERCLA. Lastly, EPA did not include emissions to ambient air from municipal and industrial waste incineration and energy recovery units in the risk evaluation, as they are regulated under section 129 of the Clean Air Act. As explained in more detail in Section 1.4.2 of the Final Risk Evaluation, EPA believes it is both reasonable and prudent to tailor TSCA Risk Evaluations when other EPA offices have expertise and experience to address specific environmental media, rather than attempt to evaluate and regulate potential exposures and risks from those media under TSCA. EPA believes that coordinated action on exposure pathways and risks addressed by other EPA-administered statutes and regulatory programs is consistent with statutory text and legislative history, particularly as they pertain to TSCA's function as a "gap-filling" statute, and also furthers EPA aims to efficiently use Agency resources, avoid duplicating efforts taken pursuant to other Agency programs, and meet the statutory deadline for completing Risk Evaluations. EPA has therefore tailored the scope of the Risk Evaluation for TCE using authorities in TSCA Sections 6(b) and 9(b)(1).
108	**PUBLIC COMMENTS:**	

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	TSCA requires that, in conducting a risk evaluation, EPA evaluate "the likely duration, intensity, frequency, and number of exposures," including exposures resulting from those allowable emissions, discharges, or releases. EPA needs to provide this analysis.	The conceptual models only included exposure pathways that are within the scope of the risk evaluation. The environmental exposure pathways covered under the jurisdiction of other EPA-administered statutes and regulatory programs are not within the scope of the risk evaluation. Clarifying language about what pathways are addressed under other statutes has been added to Section 1.4.2 of the Risk Evaluation.
49, 99	**PUBLIC COMMENTS:** Previously, the SACC indicated that "[g]eneral human population and biota exposure must be assessed for inhalation, ingestion, and dermal routes [and that] [d]ifferent sub-populations may have different extents of exposure, but each route must be assessed." • If risks have been assessed by other program offices of EPA, then EPA should present them as part of the underlying data to support this TSCA draft risk evaluation – if not, EPA must gather the data for an assessment or include an assessment based on the assumption of near-worst-case exposures.	
EPA should aggregate across COU and exposure pathways (inhalation and dermal routes; occupational and consumer)		
SACC, 47, 49, 56, 65, 74, 75, 99, 100, 104, 108	**SACC COMMENTS:** Non-consideration of aggregate exposures (*e.g.,* workers who are also consumer users; workers that may be exposed in more than one scenario) will be a standing problem unless EPA places their estimates in the context of risks from sources and pathways not included in the TSCA draft risk evaluation. Recommendation: Improve the discussion on aggregate exposure and justification for it not being performed. The issue of aggregate exposure combining inhalation and dermal routes is inadequately discussed and ignored. Recommendation: Consider aggregating dermal and inhalation exposures for consumer users when simultaneous exposures by both routes are expected. There were different opinions expressed by Committee members about aggregation of dermal and inhalation exposures. Some Committee members noted that exposures by both routes should be aggregated in all scenarios. One member noted that aggregating dermal and inhalation exposure in all cases is not warranted because if there is dermal	TSCA section 6(b)(4)(F)(ii) directs EPA to "describe whether aggregate or sentinel exposures to a chemical substance under the conditions of use were considered, and the basis for that consideration" in risk evaluations. EPA defines aggregate exposures as the combined exposures to an individual from a single chemical substance across multiple routes (*i.e.,* dermal, inhalation, or oral) and across multiple pathways (*i.e.,* exposure from different sources). 40 CFR 702.33. EPA defines sentinel exposures as the exposure from a single chemical substance that represents the plausible upper bound of exposure relative to all other exposures within a broad category of similar or related exposures. 40 CFR 702.33. EPA considered the reasonably available information and used the

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	exposure, there is almost certainly inhalation exposure, but the converse is not necessarily always true. **PUBLIC COMMENTS:** EPA failed to assess "the combined exposures to an individual from a single chemical substance across multiple routes and across multiple pathways" as required by TSCA. It failed to consider combined exposures of workers from multiple COUs, including aggregate exposure among individuals exposed both in an occupational and consumer context, at work and at home, indicating that there is insufficient information reasonably available as to the likelihood of this scenario or the relative distribution of exposures from each pathway. • EPA should use its information authorities to gain more information about these scenarios. • EPA could combine its exposure estimates for workplace COUs with those it has developed for consumer COUs (with adjustments). These aggregated exposure estimates would be representative of a large subset of workers who use (or are bystanders to the use of) TCE-containing consumer products. By defining a subgroup with high-end exposure and risk, this would enable EPA to meet its obligation under TSCA to determine unreasonable risks to "potentially exposed or susceptible subpopulations" or PESS. EPA failed to consider workers' combined exposure from multiple routes as required by TSCA. EPA recognizes that workers could readily experience exposures by both inhalation and dermal routes, including over the same time period, and states that it is essential to evaluate exposures from both of these routes in combination, including simultaneously, to assess total body burden and the associated effects. • EPA, however, dismisses employing an additivity approach to assess overall exposure with insufficient justification, and then fails to acknowledge that this will result in an underestimation of exposure. • EPA's concern about overestimating exposure is not credible.	best available science to determine whether to consider aggregate or sentinel exposures for a particular chemical. EPA has determined that using the high-end risk estimate for inhalation and dermal risks separately as the basis for the unreasonable risk determination is a best available science approach. There is low confidence, based on the weight of the scientific evidence, in the result of aggregating the dermal and inhalation risks for this chemical if EPA uses an additive approach, due to the uncertainty in the data. EPA does not have reasonably available data that could be reliably modeled for aggregating dermal exposure with other routes without a dermal compartment in the PBPK model, which would be a more accurate approach than simple additivity. Using an additive approach to aggregate risk in this case could result in an overestimate of risk. Given all the limitations that exist with the data, EPA's approach is the best available science. EPA has added language to Sections 2.3.2.6.1 and 4.4.2 describing these assumptions and uncertainties. EPA did not consider background exposure that workers, ONUs, consumers, and bystanders using products containing TCE who might be exposed to in addition to exposures from the conditions of use in the scope of the risk evaluation. Risk is likely to be elevated for individuals who experience TCE exposure in

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	• EPA has failed to consider previous SACC recommendations to combine the inhalation and dermal exposures. Risk determinations for all occupational and consumer COUs should be based upon aggregation of all exposures. Aggregation of exposures within a COU, coupled with exposures known to exist outside a COU, should always be implemented as a benchmark of a credible and responsible exposure assessment. • EPA's contrary approach of evaluating each COU in isolation is an unlawful attempt to minimize the assessment of the total risk posed by TCE and avoid regulation. EPA must examine the combined combination of all COUs to total risk and exposure and cannot determine unreasonable risk for each COU in isolation Risks to workers and consumers should be a function of the aggregate contribution of each activity and pathway to total exposure. However, the draft risk evaluation looks at each exposure pathway in isolation from others, thus underestimating total risk. The World Health Organization has warned that workers "living in the vicinity of plants emitting TCE to the air" are likely to face "higher than usual exposure levels." By looking at individual uses in isolation and ignoring the additional contributions of off-the-job exposures, EPA grossly understates TCE's total risks to workers.	multiple contexts. This may result in an underestimation of risk, and additional discussion of this underestimation is found in Sections 2.3.2.6.1 and 4.4.2. Per 40 CFR 702.47 "…EPA will determine whether the chemical substance presents an unreasonable risk of injury to health or the environment under each condition of use within the scope of the risk evaluation…." This approach in the implementing regulations for TSCA risk evaluations, is consistent with statutory text in TSCA section 6(b)(4)(A), which instructs EPA to conduct risk evaluations to determine whether a chemical substance presents an unreasonable risk "under the condition of use."
49, 56, 99, 108	**PUBLIC COMMENTS:** EPA has ignored all non-occupational baseline exposures worker experience, due to its exclusion of all exposures via environmental releases to air, water, and land. • EPA at least needs to take these into account as baseline exposures for workers even if it does not intend to assess risks from environmental releases. EPA cannot ignore real-world exposures when assessing individual risks to TCE. • For example, workers in vapor degreasing may live in industrialized	

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	areas with high ambient air levels or Superfund sites and consume TCE-contaminated drinking water. In the aggregate, TCE exposure by these workers would be significantly greater than exposure in the workplace alone and health risks (which are already alarmingly high for worker activities) would be correspondingly higher. • Because TCE exposure levels are higher for these subpopulations than for the general population, they face elevated risks of TCE-related health effects that the draft risk evaluation ignores.	
56, 65, 74, 100, 108	EPA does not dispute that failing to aggregate inhalation and dermal exposures may lead to an underestimate of exposure. EPA invokes uncertainty as its excuse for that underestimation. To the extent that there are uncertainties in an aggregating analysis, these do not support assuming exposure is less than the sum of the exposures. Uncertainty does not justify ignoring the fact that these exposures are actually experienced in combination.	
56, 108	**PUBLIC COMMENTS:** EPA did not establish that it prepared adequate aggregate or sentinel exposure assessments in its risk evaluation and failed to explain how its decision to rely on other exposure assessments can be reconciled with TSCA. • EPA has not explicitly stated whether, in identifying sentinel exposures for workers, use of personal protective equipment (PPE) was assumed, although it is clear that PPE use was assumed. • EPA should consider exposures without any PPE unless it can establish it is *always and effectively* used for a particular COU.	EPA's approach for developing exposure assessments for workers is to use the reasonably available information and expert judgement. When appropriate, in the risk evaluation, EPA will use exposure scenarios both with and without engineering controls and/or PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. While EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on

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		information and judgment underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. Additionally, in consideration of the uncertainties and variabilities in PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties. EPA has also outlined its PPE assumptions in section 5.1. Further, in the final risk evaluation for TCE, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE.
EPA should include exposure from vapor intrusion in the risk evaluation		
49, 90, 93, 99	**PUBLIC COMMENTS:** According to EPA, "TCE levels measured indoors have been directly linked to vapor intrusion," and "[v]apor intrusion is a likely significant source in situations where residences are located near soils or groundwater with high contamination levels." • ATSDR describes vapor intrusion as a "notable exposure route" and cites several studies that attributed elevated TCE indoor air levels to vapor intrusion from TCE-contaminated cleanup sites or groundwater. • TCE vapor intrusion resulting from disposal and from contaminated groundwater or soil near Ironbound facilities, which qualify as "spills, leaks, and other uncontrolled discharges" has been reported. Studies have also reported indoor air levels of TCE in residences, schools, and stores. EPA ignores this readily available data. • EPA's document detailing the rationale for incorporating subsurface vapor intrusion into the Superfund Hazard Ranking System details a statistically significant burden of sites involving vapor intrusion on low income populations (p. 30, EPA-HQ-SFUND-2010-1086-0076).	During the TCE Problem Formulation, EPA acknowledged the historic groundwater contamination and resulting vapor intrusion concerns. EPA also acknowledged that general population exposures may occur through inhalation, oral, and dermal. However, in the Risk Evaluation, EPA did not include pathways under programs of other environmental statutes, administered by EPA, for which long-standing regulatory and analytical processes already exist. EPA has determined that general population exposures due to drinking water contamination, groundwater contamination, and air emissions are under the jurisdiction of other statutes and are outside the scope of this risk evaluation. In addition, EPA determined that spills and leaks are not TSCA conditions of use as these

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	• EPA must evaluate exposures from ongoing TCE vapor intrusion in its final risk evaluation. • EPA has, or can reasonably generate or obtain, the information necessary to evaluate TCE vapor intrusion, meaning that the information is "reasonably available" under TSCA.	unintentional activities are covered by other statues, described further in Section 1.4.2. In exercising its discretion under TSCA section 6(b)(4)(D) to identify the conditions of use that EPA expects to consider in a risk evaluation, EPA believes it is important for the Agency to have the discretion to make reasonable, technically sound scoping decisions. EPA did not include legacy disposals, (*i.e.,* disposals that have already occurred), because they do not fall under the definition of conditions of use under TSCA section 3(4).
93	**PUBLIC COMMENTS:** While EPA recommends the consideration of vapor intrusion at certain federal Superfund and Resource Conservation and Recovery Act (RCRA) corrective action sites, many sites with TCE contamination from disposal are not, and will never be, remediated under Superfund or RCRA. For those sites that are, remediation is slow and depends on the identification of a financially viable responsible party, which often does not exist. • Thus, the possibility that some vapor intrusion incidents may be addressed under other laws does not alter EPA's duty to consider vapor intrusion in the TCE risk evaluation and to issue risk management rules that regulate TCE "to the extent necessary so that [this] chemical substance . . . no longer presents [unreasonable] risk" to the residents of Manufacturers Place or other residential areas exposed to TCE from vapor intrusion.	
EPA's exclusion of exposures through air is invalid		
108	**PUBLIC COMMENTS:** With >12 million pounds of TCE emitted to the air in 2014, it is absurd to treat the overall exposure through this pathway as if it were "zero."	EPA did not include the emission pathways to ambient air because releases of TCE from stationary source to ambient air are under the jurisdiction of and addressed by Section 112 of the Clean Air Act (CAA). Clarifying language about what pathways are addressed under other statutes has been added to Section 1.4.2 of the Risk Evaluation.
49, 99, 56, 108, 74	**PUBLIC COMMENTS:** Large segments of the U.S. population are likely exposed to TCE levels in air that present unreasonable risks of cancer and non-cancer effects.	EPA did not consider background exposure that workers and consumers using products

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	• Based on Integrated Risk Information System (IRIS)-determined cancer risk levels (70-year lifetime exposure) for different TCE ambient air concentrations, levels in ambient air for all locations except forests would present lifetime cancer risks above 1 in 1 million. Risks for higher levels within the range measured would exceed 1 in 100,000. • Mean ambient air levels in most locations (which range between 0.89 and 1.6 $\mu g/m^3$) would be close to the IRIS non-cancer reference concentration (RfC) of 0.0004 ppm (0.4 ppb or 2 $\mu g/m^3$), which IRIS describes as having "robust support [from] . . . estimates for multiple effects from multiple studies." For individuals exposed to ambient TCE levels near the higher end of the reported range, the RfC would be exceeded. • TCE is listed as a HAP and EPA relies on the CAA to dismiss the need to assess exposures to TCE from air emissions; however, the CAA is for individual source categories, meaning that the exposures to TCE from all sources in combination are never considered. Therefore, EPA's approach to risk evaluations under TSCA ensures that EPA never evaluates, and the public never finds out, the risk from all air emissions of TCE or any other chemical substance. The control of pollutants through CAA regulation differ in scope from EPA's authority to regulate or prohibit the production or use of these substances under TSCA. • By EPA's own account, its CAA regulation of TCE did not eliminate all risk from facilities engaged in halogenated solvent cleaning, or consider how exposure to TCE from the regulated facilities might combine with exposures from other facilities and sources to increase overall risk. • It cannot therefore be assumed that the CAA will eliminate risk to exposed populations.	containing TCE might be exposed to in addition to exposures from conditions of use in the scope of the risk evaluation. This may result in an underestimation of risk, and additional discussion of this underestimation has been added to Sections 2.3.2.6.1 and 4.4.2. The purpose of risk evaluation under TSCA is "to determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other nonrisk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator, under the conditions of use." TSCA section 6(b)(4)(A). EPA described background exposure in the uncertainties section acknowledging that the risk estimations in the Risk Evaluation may be underestimations, because background exposures and risk are not incorporated into the risk estimations for each OES. Emissions to ambient air from commercial or industrial stationary sources, or inhalation exposures of terrestrial species are managed under the jurisdiction of the Clean Air Act (CAA).
90, 108	**PUBLIC COMMENTS:** EPA's exclusion of exposure levels through the ambient air pathway, particularly near sites where people may experience greater exposure due	EPA has determined that general population exposures due to drinking water contamination,

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	to their proximity to COUs or contamination sites, will seriously underestimate the levels of exposure across the country. EPA should use its information authorities to obtain information about exposure levels experienced by the subpopulations living near COUs. • Adding to the TRI air exposure is the exposure from Superfund sites, over 50% of which include TCE as a contaminant of concern under CERLA's provisions. Elevated levels of TCE in indoor air near Superfund sites has been documented in California, and North Carolina (ROD Middlefield-Ellis-Whisman, OIG Report No. 16-P-0296).	groundwater contamination, and air emissions are under the jurisdiction of other statutes and are outside the scope of this risk evaluation. In exercising its discretion under TSCA section 6(b)(4)(D) to identify the conditions of use that EPA expects to consider in a risk evaluation, EPA believes it is important for the Agency to have the discretion to make reasonable, technically sound scoping decisions. EPA did not include legacy disposals, (*i.e.,* disposals that have already occurred), because they do not fall under the definition of conditions of use under TSCA section 3(4).
49, 99, 93	**PUBLIC COMMENTS:** According to IRIS, "TCE can be released to indoor air from use of consumer products that contain it (*i.e.,* adhesives and tapes), vapor intrusion (migration of volatile chemicals from the subsurface into overlying buildings) and volatilization from the water supply." • Consistently measured indoor levels have been shown to be higher than outdoor levels. • Several studies, including Wallace (1987), Andelman (1985), Shah and Singh (1988), Hers et al. (2001), Sapkota et al. (2005), Sexton et al. (2005), and Zhu et al. (2005), report levels that exceed a 1 in 1 million cancer risk and, at the higher end of the reported range, would exceed the IRIS RfC. • ATSDR reports that the contribution to TCE indoor levels of volatilization of contaminated drinking water is well-documented: Andelman, (1985); McKone and Knezovich (1991). • EPA has repeatedly acknowledged the risks associated with TCE vapor intrusion and has published guidance governing the calculation of vapor intrusion risks. There is no basis for EPA to exclude vapor	Unlike other EPA programs, TSCA requires chemical risk be assessed and determined for each "condition of use" and not by media (*e.g.,* indoor air). EPA did an extensive assessment of TCE in 7 consumer product categories covering 25 COU and concluded their use presented unreasonable inhalation risk (*i.e.,* from the air pathway) in all indoor uses. See Section 2.3.3 for details about the consumer risk assessments. Regarding volatilization from the water supply, EPA acknowledged the historic groundwater contamination and resulting vapor intrusion concerns in the TCE Problem Formulation. EPA also acknowledged that general population exposures may occur through inhalation, oral, and dermal routes. However, in the Risk

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	intrusion and other disposal-related TCE emissions from the draft risk evaluation. The draft risk evaluation does not look more broadly at indoor TCE air concentrations to which consumers are exposed, and overlooks the combined contributions to exposure of product use and other indoor exposure pathways like volatilization of TCE from contaminated water and intrusion of TCE vapors from contaminated soil and groundwater. This underestimates TCE risks in the indoor environment.	Evaluation, EPA did not include pathways under programs of other environmental statutes, administered by EPA, for which long-standing regulatory and analytical processes already exist.
EPA exclusion of exposures through drinking and ambient water is invalid		
SACC	**SACC COMMENTS:** Exposure from drinking water is not adequately covered in the risk assessment.	As part of the problem formulation for TCE, EPA identified exposure pathways under other environmental statutes administered by EPA, e.g., the Clean Air Act (CAA), the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA) and the Resource Conservation and Recovery Act (RCRA). As explained in more detail in Section 1.4.2 of the Final Risk Evaluation, EPA believes it is both reasonable and prudent to tailor TSCA Risk Evaluations when other EPA offices have expertise and experience to address specific environmental media, rather than attempt to evaluate and regulate potential exposures and risks from those media under TSCA. EPA believes that coordinated action on exposure pathways and risks addressed by other EPA-administered statutes and regulatory programs is consistent with statutory text and legislative history, particularly as they pertain to TSCA's function as a "gap-filling" statute, and also furthers EPA aims to efficiently use Agency resources, avoid
74, 90, 99, 108	**PUBLIC COMMENTS:** EPA ignored all exposures through drinking water despite available evidence that exposures do occur through this pathway. • The existence of a Maximum Contaminant Level (MCL) does not result in zero exposures to TCE through drinking water; EPA should analyze the real-world exposures. • EPA has not shown that the MCL of 5.0 µg/L eliminates any unreasonable risk or assessed all relevant aspects of the risk. The current MCL is outdated and not health protective. The IRIS non-cancer reference dose (RfD) is 0.5 µg/L. • The Safe Water Drinking Act (SWDA) MCL is based on non-risk factors including what is feasible (*e.g.,* with regard to treatment and monitoring) and cost. EPA cannot consider these during the risk evaluation process. • The MCL is higher than the maximum contaminant level goal (MCLG) for TCE, which is zero, indicating that in order to avoid adverse effects on human health from drinking water TCE should not be in drinking water at any level, EPA must address the risks posed by ongoing exposure to TCE at levels in drinking water below the MCL.	

	• The SWDA does not regulate all sources of water including private drinking wells; this source needs to be evaluated. • Analyzing exposure through drinking water is important to obtain an accurate estimate of the exposure of infants and children. Exceedances of the MCL have been recorded in 149 PWSs. Cancer and non-cancer risks to this subpopulation exceed EPA benchmarks for unreasonable risk, even without considering the volatilization of household water during showering and other daily activities and resulting in TCE inhalation exposure.	duplicating efforts taken pursuant to other Agency programs, and meet the statutory deadline for completing Risk Evaluations. EPA has therefore tailored the scope of the Risk Evaluation for TCE using authorities in TSCA Sections 6(b) and 9(b)(1). The conceptual models only included exposure pathways that are within the scope of the risk evaluation. The environmental exposure pathways covered under the jurisdiction of other EPA-administered statutes and regulatory programs are not within the scope of the risk evaluation. Because the drinking water exposure pathway for TCE is currently addressed in the SDWA regulatory analytical process for public water systems, EPA did not include this pathway in the risk evaluation for TCE under TSCA. In Problem Formulation, EPA also found general population exposures to TCE via underground injection, RCRA Subtitle C hazardous waste landfills, RCRA Subtitle D municipal solid waste (MSW) landfills, and on-site releases to land from industrial non-hazardous waste and construction/demolition waste landfills are under the jurisdiction of and addressed by other EPA-administered statutes and associated regulatory programs. EPA did not include Superfund on-site releases to the environment, as they are under the jurisdiction of CERCLA. Lastly, EPA
SACC	**SACC COMMENTS:** Exclusion of groundwater on the basis of regulation under clean water or safe drinking water statutes is erroneous, because private wells are not regulated under the Clean Water Act (CWA) or SDWA.	
108	**PUBLIC COMMENTS:** EPA ignores exposures through ambient water citing regulation through the CWA. • Not all states have updated their criteria to reflect the current CWA criteria and are using less stringent standards. Therefore, EPA cannot rely on the CWA recommendations to assume that risks are adequately managed. • EPA has not demonstrated that the established criteria reflect the current best available science. • EPA has not acknowledged the ongoing uncertainty surrounding the definition of "waters of the United States" regulated under the CWA including the regulatory reach of the CWA as well as compliance and enforcement activities. EPA cannot assume that all ambient water is adequately managed under the CWA when EPA itself expresses ongoing uncertainty over the jurisdictional reach of the CWA. In the draft risk evaluation, EPA describes monitoring data and published literature showing that TCE is present in surface water. EPA's own modeling shows that TCE is present in surface water at significant	

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	concentrations. EPA cannot assume that TCE has nonexistent exposure through ambient water. • EPA should examine and summarize that exposure information when evaluating the risks presented by TCE; if that information is insufficient, EPA should use its authorities to require the development of additional needed information. • EPA must analyze the ambient water pathway in the risk evaluations.	did not include emissions to ambient air from municipal and industrial waste incineration and energy recovery units in the risk evaluation, as they are regulated under section 129 of the Clean Air Act. Clarifying language about what pathways are addressed under other statutes has been added to Section 1.4.2 of the Risk Evaluation.
107	**PUBLIC COMMENTS:** EPA's failure to include drinking water exposure results in an underestimation of exposure and ultimately, risk. It is easier, more effective, and more equitable to control pollutants at the source, where they are highly concentrated, than it is to remove them at the consumer's expense after they have entered a water body or supply source. EPA has the authority under TSCA to control the introduction into the environment of contaminants such as TCE that degrade water quality and increase the cost of water treatment.	
EPA exclusion of exposures through disposal is invalid		
108	**PUBLIC COMMENTS:** EPA limited analysis of exposure from "Process Solvent Recycling and Worker Handling of Wastes," to workers and occupational non-users (ONUs). General population exposure to all ambient air, land disposal, and waste incineration pathways were excluded as well as exposures from all disposal-related pathways and associated activities (*e.g.,* collection, processing, storage, and transport) due to regulation of disposal under the RCRA, CAA, SDWA, and various state programs. • EPA has not established or shown that disposal regulations "adequately assess and effectively manage exposures." • EPA recognized that not all disposal occurs in RCRA Subtitle C landfills, and that other disposal sites do not meet the requirements of Subtitle C. Some state programs don't include requirements for liners to limit release of landfill leachate. • EPA acknowledged that enforcement and regulation under RCRA is inconsistent, so it cannot simply assume that RCRA implementation	EPA evaluated and considered the impact of existing laws and regulations (*e.g.,* regulations on landfill disposal, design, and operations) in the problem formulation step to determine what, if any future analysis might be necessary as part of the risk evaluation. During problem formulation EPA analyzed the TRI data and examined the definitions of elements in the TRI data to determine the level of confidence that a release would result from certain types of disposal to land (*e.g.,* RCRA Subtitle C hazardous landfill and Class I underground Injection wells) and incineration. EPA also examined how TCE is treated at industrial facilities. EPA did not include emissions to

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	provides a basis for ignoring exposures. • Congress specifically directed EPA to analyze the risks of chemicals presented "under the conditions of use," and Congress consciously decided to specify that "disposal" is a COU under TSCA. "Conditions of use" expressly includes "the circumstances under which a chemical substance is intended, known, or reasonably foreseen to be to be manufactured, processed, distributed in commerce, used, or disposed of."	ambient air from commercial and industrial stationary sources, which are under the jurisdiction of and addressed by Section 112 of the Clean Air Act. EPA did not include emissions to ambient air from municipal and industrial waste incineration and energy recovery units in the risk evaluation, as they are regulated under section 129 of the Clean Air Act. EPA did not include disposal to underground injection, RCRA Subtitle C hazardous waste landfills, RCRA Subtitle D municipal solid waste (MSW) landfills, and on-site releases to land from industrial non-hazardous waste and construction/demolition waste landfills in this Risk Evaluation. EPA did not include Superfund on-site releases to the environment, as they are under the jurisdiction of CERCLA. These methods of disposal fall under the jurisdiction of and are addressed by other EPA-administered statutes and associated regulatory programs. As explained in more detail in Section 1.4.2 of the Final Risk Evaluation, EPA believes it is both reasonable and prudent to tailor TSCA Risk Evaluations when other EPA offices have expertise and experience to address specific environmental media, rather than attempt to evaluate and regulate potential exposures and risks from those media under TSCA. EPA believes that coordinated action on exposure pathways and risks addressed by other EPA-administered statutes and regulatory programs is

		consistent with statutory text and legislative history, particularly as they pertain to TSCA's function as a "gap-filling" statute, and also furthers EPA aims to efficiently use Agency resources, avoid duplicating efforts taken pursuant to other Agency programs, and meet the statutory deadline for completing Risk Evaluations. EPA has therefore tailored the scope of the Risk Evaluation for TCE using authorities in TSCA Sections 6(b) and 9(b)(1).
108	**PUBLIC COMMENTS:** There are almost 1,300 instances of required rules for which various state hazardous waste programs have not been authorized. When states have out-of-date hazardous waste programs, citizens in different states are unevenly protected from hazardous waste-related risks. • EPA cannot rely on assumptions of consistent implementation and enforcement of RCRA to ensure adequate management. • For EPA to treat these exposure levels as "zero" when they exist does not comport with the best available science. • EPA should use their authority to obtain additional information about the exposures arising from disposal for TCE.	See below response regarding the Land Disposal Program Flexibility Act of 1996, codified at RCRA section 3010a(c)(5) and (6).
EPA must consider exposures in tribal communities		
104	**PUBLIC COMMENTS:** Environmental statutes do not guarantee protection from exposures, particularly in the case of tribes, which may be disproportionately impacted. Disposal circumstances on tribal lands are different from those of urban areas with municipal landfills. In the case of many tribal and rural communities, the disposal site may be in close proximity to residents, be unlined, open access, or include open burning as a management practice. These present multiple exposure pathways and routes for intake and uptake. • EPA states that "Studies clearly associated with releases from Superfund sites, improper disposal methods, landfills were	The commenter appears to be describing aspects of the Land Disposal Program Flexibility Act of 1996, codified at RCRA section 3010a(c)(5) and (6). The law directed EPA to provide additional flexibility to approved states for landfills that receive 20 tons or less of municipal solid waste per day. The additional flexibility applies to alternative frequencies of daily cover, frequencies of methane monitoring, infiltration layers for final cover, and means for

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	considered not to meet the PECO statement and [were] excluded from data evaluation and extraction." Leachate samples were excluded because they were considered an "off-topic" media. • TCE is considered hazardous waste under RCRA but many tribal communities do not have access to Subtitle C landfills. There is not a single Subtitle C landfill in the State of Alaska. Tribes experience exposures even where responsibility rests on other environmental statutes. • EPA should revise this risk evaluation to include TCE releases from landfills, including those that are characteristic of tribal communities. • Disposal is a main route for TCE to enter the environment; it is unacceptable to exclude disposal, and the resulting exposures, from consideration.	demonstrating financial assurance. Section 3010a(c)(6). Further, under section 3010a(c)(5), if the Alaska governor certifies that application of the requirements for groundwater monitoring, siting, or corrective action to a solid waste landfill unit of a Native village, or a unit located in or near a small, remote Alaska village, would be infeasible, would not be cost-effective, or would be otherwise inappropriate because of the remote location of the unit, Alaska may exempt the unit from some or all of those requirements. It is not at all clear to EPA that Congress intended for TSCA to override the flexibilities specifically provided for small municipal solid waste landfills and the additional flexibilities specifically provided to Alaska in the Land Disposal Program Flexibility Act of 1996. EPA believes that the 1996 Act represents Congressional recognition that the RCRA Subtitle D program is not always feasible, or practicable, for the small landfills covered by the Act, and the additional flexibility provided by the Act is therefore necessary and appropriate.
104	**PUBLIC COMMENTS:** EPA must consider aggregate and cumulative exposures for tribal communities. A single person may be a landfill worker, an occupational bystander, and a near-facility general population, as well as a consumer. They will likely derive their food and water, including untreated water, near-source. Such scenarios are the norm for landfill workers in the over 200 Alaska tribal communities.	EPA did not consider aggregate or background exposure that workers, ONUs, consumers, or bystanders using products containing TCE might be exposed to in addition to exposures from the conditions of use in the scope of the risk evaluation because there is insufficient information reasonably available as to the likelihood of this scenario or the relative distribution of exposures from each pathway.

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		This may result in an underestimation of risk, and EPA acknowledges that risk is likely to be elevated for individuals who experience TCE exposure in multiple contexts. Additional discussion of this issue has been added to Sections 2.3.2.6.1, 2.3.2.2.1, and 4.4.2.
104	**PUBLIC COMMENTS:** Native Americans are more highly exposed to contaminants with environmental fate and transport than other populations because their lifeways revolve around environmental activities for dietary sustenance, socio-cultural activities, ceremonial and spiritual purposes, recreation, and general well-being. Tribal lifeways can lead to chronic exposures to toxins in the environment, due to longer duration and higher frequency of exposures, and a higher cumulative dose from multiple exposure pathways. Native Americans experience significant health disparities from the general population and the practice of leaving them out of any protections will only contribute to further health disparities.	EPA recognizes that Native Americans have unique lifeways and has considered established differences in patterns in relevant exposure pathways (*e.g.,* increased fish consumption). However, general population exposure pathways were not included in the scope of the risk evaluation as discussed in Section 1.4.2 and a review of reasonably available information did not produce data for establishing a differential experience for the evaluated exposure pathways, namely occupational and consumer activities. An additional statement about the uncertainty associated with subpopulations patterns of use has been added to Section 2.3.2.6.2.
104	**PUBLIC COMMENTS:** EPA is urged to consider data submitted by the Tribe that produced it. Where data are not available, modeling should be employed so that all significant Tribal exposures are captured. Evaluation of chemicals should then include tribal peoples' multiple unique exposures.	
EPA must consider exposures due to accidental releases		
56, 108	**PUBLIC COMMENTS:** EPA does not consider risks of exposure due to potential accidental releases. This risk is "reasonably foreseen" and EPA has authority to mandate steps to reduce those risks. EPA needs to give more consideration to the potential for accidental releases.	Accidental releases, spills and leaks generally are not included within the scope of a TSCA risk evaluation because in general they are not considered to be circumstances under which a chemical substance is intended, known or reasonably foreseen to be manufactured, processed, distributed, used, or disposed of. To the extent there may be potential exposure from accidents, EPA is also declining to evaluate
56, 90, 100, 108	**PUBLIC COMMENTS:** EPA excluded exposures from spills and leaks. • There are many documented spills of TCE both within the workplace and to the environment. These exposures should be considered "reasonably foreseen" under TSCA.	

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	EPA should evaluate exposures and risks posed by reasonably foreseen spills and other occupational releases of TCE.	environmental exposure pathways addressed by another EPA-administered statutes and associated regulatory programs. First, EPA does not identify TCE accidental releases, spills and leaks as "conditions of use." EPA does not consider TCE accidental releases, spills and leaks to constitute circumstances under which TCE is manufactured, processed, distributed, used, or disposed of, within TSCA's definition of "conditions of use." Congress specifically listed discrete, routine chemical lifecycle stages within the statutory definition of "conditions of use" and EPA does not believe it is reasonable to interpret "circumstances" under which TCE is manufactured, processed, distributed, used, or disposed of to include uncommon and unconfined accidents, spills or leaks for purposes of the statutory definition. Further, EPA does not generally consider accidental releases, spills and leaks to constitute "disposal" of a chemical for purposes of identifying a COU in the conduct of a risk evaluation. In addition, even if accidents, spills or leaks of TCE could be considered part of the listed lifecycle stages of TCE, EPA has "determined" that accidents, spills and leaks are not circumstances under which TCE is intended, known or reasonably foreseen to be manufactured, processed, distributed, used, or disposed of, as provided by TSCA's definition

		of "conditions of use," and EPA is therefore exercising its discretionary authority under TSCA section 3(4) to exclude TCE accidental releases, spills and leaks from the scope of the TCE risk evaluation. The exercise of that authority is informed by EPA's experience in developing scoping documents and risk evaluations, and on various TSCA provisions indicating the intent for EPA to have some discretion on how best to address the demands associated with implementation of the full TSCA risk evaluation process. Specifically, since the publication of the Risk Evaluation Rule, EPA has gained experience by conducting ten risk evaluations and designating forty chemical substances as low- and high-priority substances. These processes have required EPA to determine whether the case-specific facts and the reasonably available information justify identifying a particular activity as a "condition of use." With the experience EPA has gained, it is better situated to discern circumstances that are appropriately considered to be outside the bounds of "circumstances… under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of" and to thereby meaningfully limit circumstances subject to evaluation. Because of the expansive and potentially boundless impacts that could result from including accidents, spills and leaks as part of the risk evaluation (*e.g.,* due to the unpredictable and irregular scenarios that

		would need to be accounted for, including variability in volume, frequency, and geographic location of accidents, spills and leaks; potential application across multiple exposure routes and pathways affecting myriad ecological and human receptors; and far-reaching analyses that would be needed to support assessments that account for uncertainties but are based on best available science), which could make the conduct of the risk evaluation untenable within the applicable deadlines, accidents, spills and leaks are determined not to be circumstances under which TCE is intended, known or reasonably foreseen to be manufactured, processed, distributed, used, or disposed of, as provided by TSCA's definition of "conditions of use." Exercising the discretion to not identify accidents, spills and leaks of TCE as a COU is consistent with the discretion Congress provided in a variety of provisions to manage the challenges presented in implementing TSCA risk evaluation. See *e.g.,* TSCA sections 3(4), 3(12), 6(b)(4)(D), 6(b)(4)(F). In particular, TSCA section 6(b)(4)(F)(iv) instructs EPA to factor into TSCA risk evaluations "the likely duration, intensity, frequency, and number of exposures under the conditions of use….," suggesting that activities for which duration, intensity, frequency, and number of exposures cannot be accurately predicted or calculated based on reasonably available information,

		including accidents, were not intended to be the focus of TSCA risk evaluations. And, as noted in the preamble to the Risk Evaluation Rule, EPA believes that Congress intended there to be some reasonable limitation on TSCA risk evaluations, expressly indicated by the direction in TSCA section 2(c) to "carry out [TSCA] in a reasonable and prudent manner." For these reasons, EPA is exercising this discretion to not consider accidents, spills and leaks of TCE to be COUs. Second, even if TCE accidents, spills and leaks could be identified as exposures from a COU in some cases, these are generally not forms of exposure that EPA expects to consider in risk evaluation. TSCA Section 6(b)(4)(D) requires EPA, in developing the scope of a risk evaluation, to identify the hazards, exposures, conditions of use, and potentially exposed or susceptible subpopulations the Agency "expects to consider" in a risk evaluation. This language suggests that EPA is not required to consider all conditions of use, hazards, or exposure pathways in risk evaluations. EPA has chosen to tailor the scope of the risk evaluation to exclude spills and leaks in order to focus analytical efforts on those exposures that present the greatest potential for risk. In the problem formulation documents for many of the first 10 chemicals undergoing risk

		evaluation, EPA applied the same authority and rationale to certain exposure pathways, explaining that "EPA is planning to exercise its discretion under TSCA 6(b)(4)(D) to focus its analytical efforts on exposures that are likely to present the greatest concern and consequently merit a risk evaluation under TSCA...." This approach is informed by the legislative history of the amended TSCA, which supports the Agency's exercise of discretion to focus the risk evaluation on areas that raise the greatest potential for risk. See June 7, 2016 Cong. Rec., S3519-S3520. In addition to TSCA section 6(b)(4)(D), the Agency also has discretionary authority under the first sentence of TSCA section 9(b)(1) to "coordinate actions taken under [TSCA] with actions taken under other Federal laws administered in whole or in part by the Administrator." TSCA section 9(b)(1) provides EPA authority to coordinate actions with other EPA offices, including coordination on tailoring the scope of TSCA risk evaluations to focus on areas of greatest concern rather than exposure pathways addressed by other EPA-administered statutes and regulatory programs, which does not involve a risk determination or public interest finding under TSCA section 9(b)(2). EPA has already tailored the scope of this risk evaluation using such discretionary authorities with respect to exposure pathways covered under the jurisdiction of other EPA-administered

		statutes and associated regulatory programs (see section 1.4.2). Following coordination with EPA's Office of Land and Emergency Management (OLEM), EPA has found that exposures of TCE from accidents, spills and leaks fall under the jurisdiction of RCRA. See 40 CFR 261.33(d) (defining in part a hazardous waste as "any residue or contaminated soil, water or other debris resulting from the cleanup of a spill into or on any land or water of any commercial chemical product or manufacturing chemical intermediate having the generic name listed [40 CFR 261.33(e) or (f)], or any residue or contaminated soil, water or other debris resulting from the cleanup of a spill, into or on any land or water, of any off-specification chemical product and manufacturing chemical intermediate which, if it met specifications, would have the generic name listed in [40 CFR 261.33(e) or (f)]"); 40 CFR 261.33(f) (listing TCE as hazardous waste no. U080). As a result, EPA believes it is both reasonable and prudent to tailor the TSCA risk evaluation for TCE by declining to evaluate potential exposures from accidents, spills and leaks, rather than attempt to evaluate and regulate potential exposures from accidents under TSCA. Releases from municipal landfills are regulated under RCRA. As explained in more detail in Section 1.4.2, EPA believes that coordinated

		action on exposure pathways and risks addressed by other EPA-administered statutes and regulatory programs is consistent with statutory text and legislative history, particularly as they pertain to TSCA's function as a "gap-filling" statute, and also furthers EPA aims to efficiently use Agency resources, avoid duplicating efforts taken pursuant to other Agency programs, and meet the statutory deadline for completing risk evaluations. EPA does not expect exposure to consumers from disposal of consumer products. It is anticipated that most products will be disposed of in original containers, particularly those products that are purchased as aerosol cans. As described in section 1.4.2 EPA is not evaluating on-site releases to land from RCRA Subtitle D municipal solid waste (MSW) landfills or exposures of the general population from such releases in the TSCA evaluation because they are adequately addressed by other EPA statutes. Disposal of household waste to municipal landfills is covered under the jurisdiction of RCRA as discussed in section 1.4.2. Additionally, the following has been added to Section 2.4.2.2 discussing possible consumer Exposure Routes: "EPA does not expect exposure to consumers from disposal of consumer products. It is anticipated that most products will be disposed of in original

		containers, particularly those products that are purchased as aerosol cans."
EPA cannot rely on other authorities due to numerous problems with compliance, implementation, and enforcement		
108	**PUBLIC COMMENTS:** State enforcement of these environmental statutes is inconsistent and often deficient. Even where enforcement has been consistently deficient, EPA has generally not de-authorized states. Implementation and enforcement of these statutes remains deficient in a number of states, resulting in continued excessive exposure to these chemicals through air, water, and land. These exposures must be assessed under TSCA. Specific examples of deficiencies under each of the statutes that EPA cites as justification for excluding multiple exposure pathways follow. SWDA: • EPA often receives unreliable data from states. EPA relies on state data to determine whether there is compliance with the SDWA. Without reliable data, EPA has no way to verify that the requirements of the SDWA are being met by the states. • Due to understaffing, SWDA violations doubled in Pennsylvania from 4,298 to 7,922. CWA: • Over half of assessed U.S. river and stream miles violate state water quality standards. EPA's own analysis, provided below, indicates that waters remained impaired throughout the United States, despite the CWA standards. • EPA published the Annual Noncompliance Report (2015) indicates enforcement actions were taken on only 8.9% of violations. CAA: • The OIG found performance varied significantly across the country; particular issues in FL, NC, and OH were highlighted. RCRA: • There are serious state enforcement problems with RCRA in addition to issues with accurate identification and documentation of	EPA did not consider background exposure that workers, ONUs, consumers, and bystanders using products containing TCE might be exposed to in addition to exposures from conditions of use in the scope of the risk evaluation. This may result in an underestimation of risk, and additional discussion of this underestimation has been added to the document in the uncertainties section. See section 1.4.2 of the risk evaluation regarding EPA's approach to exposure pathways and risks addressed by other EPA-administered statutes. EPA evaluated and considered the impact of existing laws and regulations (*e.g.,* regulations on landfill disposal, design, and operations) in the problem formulation step to determine what, if any future analysis might be necessary as part of the risk evaluation. During problem formulation EPA analyzed the TRI data and examined the definitions of elements in the TRI data to determine the level of confidence that a release would result from certain types of disposal to land (*e.g.,* RCRA Subtitle C hazardous landfill and Class I underground Injection wells) and incineration. EPA also

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	violations. Reduced EPA enforcement provides even less assurance that exposures through the excluded pathways are being effectively managed. Under the current Administration, enforcement of these environmental statutes has been significantly curbed. EPA cannot legally ignore exposures that occur under other EPA-administered statutes and treating exposures that are known to occur in the world as nonexistent is arbitrary and capricious.	examined how TCE is treated at industrial facilities. EPA did not include emissions to ambient air from commercial and industrial stationary sources, which are under the jurisdiction of and addressed by Section 112 of the Clean Air Act. EPA did not include emissions to ambient air from municipal and industrial waste incineration and energy recovery units in the risk evaluation, as they are regulated under section 129 of the Clean Air Act. EPA did not include disposal to underground injection, RCRA Subtitle C hazardous waste landfills, RCRA Subtitle D municipal solid waste (MSW) landfills, and on-site releases to land from industrial non-hazardous waste and construction/demolition waste landfills in this Risk Evaluation. EPA did not include Superfund on-site releases to the environment, as they are under the jurisdiction of CERCLA. These methods of disposal fall under the jurisdiction of and are addressed by other EPA-administered statutes and associated regulatory programs. As explained in more detail in Section 1.4.2 of the Final Risk Evaluation, EPA believes it is both reasonable and prudent to tailor TSCA Risk Evaluations when other EPA offices have expertise and experience to address specific environmental media, rather than attempt to evaluate and regulate potential exposures and risks from those media under TSCA. EPA believes that coordinated action on exposure

		pathways and risks addressed by other EPA-administered statutes and regulatory programs is consistent with statutory text and legislative history, particularly as they pertain to TSCA's function as a "gap-filling" statute, and also furthers EPA aims to efficiently use Agency resources, avoid duplicating efforts taken pursuant to other Agency programs, and meet the statutory deadline for completing Risk Evaluations. EPA has therefore tailored the scope of the Risk Evaluation for TCE using authorities in TSCA Sections 6(b) and 9(b)(1).
108	**PUBLIC COMMENTS:** • In its proposed 2020 budget, the current Administration sought a 31% reduction in funding for EPA. This reduction would affect EPA's enforcement budget and the resources available to ensure enforcement of the statutes. EPA cannot rely on its actions under other authorities when EPA has itself taken steps to ensure that those authorities are not adequately addressing the risks presented. • Under the current Administration, enforcement of environmental statutes has been significantly curbed. Management at EPA has directed EPA investigators to seek authorization before asking companies to conduct testing or sampling under the CAA, RCRA, or CWA. The memo also states that investigators need authorization if they do not have information specific to a company that it may have violated the law, or if state authorities objected to the tests. EPA budget cuts are also expected to affect EPA's enforcement budget. • EPA has taken steps in to improve state programs, but implementation/enforcement of these statutes remains deficient resulting in continued excessive exposure to chemicals through air, water, and land. EPA cannot rely on other statutes and must assess exposures on their real-world existence.	Thank you for your comment. Per 15 U.S.C § 2605, EPA is required to prioritize, evaluate and manage unreasonable risks of chemical substances and mixtures.

EPA should coordinate with other statutes		
108	**PUBLIC COMMENTS:** TSCA provides that EPA "shall coordinate *actions* taken under [TSCA] with *actions* taken under other Federal laws administered in whole or in part by the Administrator." This does not contemplate EPA excluding exposures from the analyses prepared under TSCA.	The conceptual models only included exposure pathways that are within the scope of the risk evaluation. The environmental exposure pathways covered under the jurisdiction of other EPA-administered statutes and regulatory programs are not within the scope of the risk evaluation. As explained in more detail in Section 1.4.2 of the Final Risk Evaluation, EPA believes it is both reasonable and prudent to tailor TSCA Risk Evaluations when other EPA offices have expertise and experience to address specific environmental media, rather than attempt to evaluate and regulate potential exposures and risks from those media under TSCA. EPA believes that coordinated action on exposure pathways and risks addressed by other EPA-administered statutes and regulatory programs is consistent with statutory text and legislative history, particularly as they pertain to TSCA's function as a "gap-filling" statute, and also furthers EPA aims to efficiently use Agency resources, avoid duplicating efforts taken pursuant to other Agency programs, and meet the statutory deadline for completing Risk Evaluations. EPA has therefore tailored the scope of the Risk Evaluation for TCE using authorities in TSCA Sections 6(b) and 9(b)(1).
103	**PUBLIC COMMENTS:** EPA should be more transparent about its inter- and intra-agency consultation and coordination to inform the risk evaluation. • EPA should provide more information in its scoping documents and	In the 2017 Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act (82 FR 33726, July 20,

	draft risk evaluations about how it determines whether existing regulations under other statutes are adequate to address potential risks associated with a chemical under certain COU. It is recommended that EPA OPPT convene a broader discussion with EPA's other program offices about how OPPT can: • Better understand the regulatory requirements and processes of the various environmental statutes under EPA's purview; • Reach agreement with other program offices on the criteria to use to determine when and under what circumstances TSCA evaluations should address air, water, and other waste pathways under the COU of a high-priority chemical; and • Establish better approaches for coordinating with each program office to improve environmental protection under each statutory authority more efficiently and without duplication.	2017), EPA committed to, by codifying, interagency collaboration to give the public confidence that EPA will work with other agencies to gain appropriate information on chemical substances. This is an ongoing deliberative process and EPA is not obligated to provide descriptions of predecisional and deliberative discussions or consultations with other federal agencies. In the interest of continuing to have open and candid discussions with our interagency partners, EPA is not intending to include the content of those discussions in the risk evaluation.
103	**PUBLIC COMMENTS:** TSCA contemplates consultation between EPA and the Occupational Safety and Health Administration (OSHA) and authorizes OSHA to decide whether it agrees with EPA's risk determination concerning worker health. EPA has failed to include any discussion of its coordination/consultation with OSHA on its approaches, considerations, and conclusions in the risk evaluation. EPA should include such a discussion in the final TCE risk evaluation.	EPA consults regularly with its federal partners and will consult with state agencies if they are known to have relevant occupational exposure data. Additionally, EPA conferred with OSHA and NIOSH during interagency review and their contributions during review are reflected in both the Draft and Final Risk Evaluation. EPA regularly engages with OSHA along with its other federal partners. However, it should be noted that under section 6 of TSCA, EPA is not mandated to consult with OSHA. Under section 9(a) of TSCA, the Administrator may determine it is appropriate, after making an unreasonable risk finding, to refer an action to OSHA, but the Agency is not mandated to do so. Regarding monitoring data from state agencies and industry, EPA has considered the reasonably
61	**PUBLIC COMMENTS:** EPA should provide the SACC with all of the materials and communications sent from OSHA and NIOSH to EPA for TCE and other chemicals.	

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		available data, including from states, and has provided several opportunities for all entities to submit workplace monitoring data or other information for consideration in the risk evaluation.
COUs assessed are not valid/complete; use of qualitative approach for some COUs		
SACC	**SACC COMMENTS:** EPA should attempt to get information on use of products directly (from distributors, retailers, etc.) as an alternative means to obtain market penetration information. For some uses (*e.g.,* dry cleaning, metal working fluids, and others), the number of vendors is not overwhelming. Contacting these vendors for information would more fully inform the risk evaluation.	As noted in the document entitled EPA's Responses to Public Comments Received on the Scope Documents for the First Ten Chemicals for Risk Evaluation under TSCA, EPA-HQ-OPPT-2016-0723-0067, EPA conducted extensive and varied data gathering activities for each of the first 10 chemicals, including: • Extensive and transparent searches of public databases and sources of scientific literature, government and industry sector or other reports; • Searches of EPA TSCA 8(e), Chemical Data Reporting, and other EPA information holdings; and CBI submission holdings; • Searches for Safety Data Sheets (SDSs) using the internet, EPA Chemical and Product Categories (CPCat) data, the National Institute for Health's (NIH) Household Product Database, and other resources in which SDS could be found; • Preparation of a market analysis using proprietary databases and repositories; • Outreach meetings with chemical manufacturers, processors, chemical users,

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		non-governmental organizations, trade organizations, and other experts, including other State and Federal Agencies (*e.g.,* Dept of Defense, NASA, OSHA, NIOSH, FDA and CPSC); and • Publication of conditions of use documents, scope documents, and problem formulation documents to solicit information generally from industry, nongovernmental organizations, and the public. These sources provided sufficient information to conduct the risk evaluation and to make determinations on whether conditions of use pose an unreasonable risk. Information on market penetration would not change those findings and, while there are limited vendors collecting information from them is not necessarily straight forward. EPA cannot mandate that vendors provide market penetration information and this type of information is often considered to be sensitive and claimed as confidential business information. Also, when collecting similar information by more than nine entities, EPA is obligated (under the Paperwork Reduction Act) to develop an Information Collection Request which the schedule for the development of the Risk Evaluation did not allow.
98	**PUBLIC COMMENTS:** TSCA does not authorize EPA to identify particular COUs and make individualized determinations as to whether each COU, rather than each	Per 40 CFR 702.47 "…EPA will determine whether the chemical substance presents an unreasonable risk of injury to health or the

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	chemical, presents an unreasonable risk. This underestimates risks posed by a chemical by artificially segmenting the analysis.	environment under each condition of use within the scope of the risk evaluation…." This approach in the implementing regulations for TSCA risk evaluations, is consistent with statutory text in TSCA section 6(b)(4)(A), which instructs EPA to conduct risk evaluations to determine whether a chemical substance presents an unreasonable risk "under the condition of use."
108	**PUBLIC COMMENTS:** EPA assertion that it has authority to ignore COUs under other agencies' jurisdiction is incorrect. EPA's Risk Evaluation Rule does not grant EPA discretion to exclude COUs. The relevant provisions "unambiguously do not grant EPA the discretion" to pick-and-choose COUs for inclusion and therefore, the assertion of discretion to exclude COUs in the preamble meaningless. • EPA must also consider all hazards and all exposures under the COU. None of these duties are qualified or provide an authority for EPA to exclude hazards or sources of exposures from analysis. EPA's arguments for excluding certain COUs cannot be extended to exclude consideration of exposures and hazards.	As explained in more detail in section 1.4.2 of the risk evaluation, EPA believes it is both reasonable and prudent to tailor TSCA risk evaluations when other EPA offices have expertise and experience to address specific environmental media, rather than attempt to evaluate and regulate potential exposures and risks from those media under TSCA. EPA believes that coordinated action on exposure pathways and risks addressed by other EPA-administered statutes and regulatory programs is consistent with statutory text and legislative history, particularly as they pertain to TSCA's function as a "gap-filling" statute, and also furthers EPA aims to efficiently use Agency resources, avoid duplicating efforts taken pursuant to other Agency programs, and meet the statutory deadline for completing risk evaluations. EPA has therefore tailored the scope of the risk evaluation for TCE using authorities in TSCA sections 6(b) and 9(b)(1).
94, 101	**PUBLIC COMMENTS:**	

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	There is a central flaw in EPA's exposure assessments for TCE use as feedstock or reactant or release as byproduct in intermediate operations. There are essential differences between TCE unintentionally produced as a byproduct in EDC manufacturing and the intentional production of TCE. EPA's draft risk evaluation for TCE fails to distinguish these different manufacturing scenarios as separate COUs. Contrary to EPA's assumption, these are not comparable to the manufacture of TCE itself. When TCE is used as a feedstock or process agent, as in the manufacture of HFC-134a, it is "used and entirely consumed (except for trace quantities)." Exposure data submitted by fluorocarbon producers should confirm this. • During the majority of time TCE is present only in closed vessels or process equipment with no dermal contact. • Small magnitude exposures during short-term tasks can occur in unit operations and maintenance activities. This is usually a mixture of residuals from the process and not neat TCE. The duration of active liquid contact is also typically short (*e.g.,* minutes) and diminishes once the equipment has been drained. • Based on typical industrial hygiene practices, the use of gloves achieves much greater protection than the default assumptions that were used in the draft risk evaluation for manufacturing and use as process reactants. • Gross or continuous exposures would not be consistent with required chemical handling programs in such facilities. Some EDC companies have commercial ethylene chlorination units and manufacture TCE as a finished product. These facilities can transfer heavy end liquids from the EDC purification to that process as a feedstock, but that process should be assessed in this risk evaluation as part of the primary production of TCE, not as part of EDC. Unintended yields of TCE in manufacturing EDC are recovered in light and heavy ends and primarily used as feedstocks to make HCl or other chlorinated organics, or destroyed on site and should be considered a low exposure, site-limited impurity.	EPA will address on a case-by-case basis circumstances where the chemical substance subject to risk evaluation is unintentionally present as an impurity, or as a byproduct, resulting from a process for another chemical substance undergoing risk evaluation. In this instance, EPA included additional language in the final scope document for 1,2-dichloroethane (107-06-2) to indicate that the byproduct TCE (79-01-6) formed during the manufacture of 1,2-dichloroethane will be addressed in the 1,2-dichloroethane risk evaluation. EPA believes that the regulatory tools under TSCA section 6(a) are better suited to address any unreasonable risks that might arise from these activities through regulation of the activities that generate 1,2-dichloroethane than they are to addressing them through direct regulation of TCE. Inhalation monitoring data from manufacturing facilities were used as surrogate for other conditions of use. This data was chosen as TCE concentrations for these conditions of use would be similar to manufacturing, and TCE exposures during unloading would be comparable in magnitude to TCE loading following manufacture. Following publication of the draft risk evaluation, one industry stakeholder that uses TCE as a feedstock in the manufacture of refrigerants provided occupational exposure

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101	**PUBLIC COMMENTS:** EPA's risk evaluation must recognize that operations and data from facilities intentionally manufacturing TCE are foundationally different than operation and occupational exposures during EDC manufacturing where TCE is unintentionally produced. • During EDC production, a combination of engineering and administrative controls are used to protect workers from exposure to TCE. Aside from fugitive emissions, the only other time possible exposure may occur is during maintenance. For this material, all first line breaks are completed using breathing air and line break suits. • EPA's dermal exposure modeling of one exposure event per day to TCE in liquid form at 99-100% concentration is a massive overestimate of dermal exposure to TCE during EDC manufacturing. Similarly, the potential for inhalation exposure is significantly reduced by the much lower concentration of TCE in all process streams. • EPA must correct its draft risk evaluation and assess the production of TCE as a byproduct in EDC production as a separate COU, considering the low levels of TCE in these facilities. Because EPA did not apply available data for byproduct production operations, the calculations and unreasonable risk conclusion for the production of TCE during EDC manufacture are erroneous and unsupported.	information which was added to the manufacturing data. As a result, occupational exposure estimates for three OES have been revised in the final risk evaluation. As noted in the document entitled EPA's Responses to Public Comments Received on the Scope Documents for the First Ten Chemicals for Risk Evaluation under TSCA (EPA-HQ-OPPT-2016-0723-0067), EPA conducted extensive and varied data gathering activities for each of the first 10 chemicals, including: • Extensive and transparent searches of public databases and sources of scientific literature, government and industry sector or other reports; • Searches of EPA TSCA 8(e), Chemical Data Reporting, and other EPA information holdings; and CBI submission holdings; • Searches for Safety Data Sheets (SDSs) using the internet, EPA Chemical and Product Categories (CPCat) data, the National Institute for Health's (NIH) Household Product Database, and other resources in which SDS could be found; • Preparation of a market analysis using proprietary databases and repositories; • Outreach meetings with chemical manufacturers, processors, chemical users, non-governmental organizations, trade organizations, and other experts, including

		other State and Federal Agencies (*e.g.,* Dept of Defense, NASA, OSHA, NIOSH, FDA and CPSC); and • Publication of conditions of use documents, scope documents, and problem formulation documents to solicit information generally from industry, nongovernmental organizations, and the public. Inhalation monitoring data from facilities manufacturing TCE were used as surrogate for other conditions of use such as refrigerants manufacturing. Following publication of the draft risk evaluation, one industry stakeholder that uses TCE as a feedstock in the manufacture of refrigerants provided occupational exposure information which was added to the manufacturing data. As a result, occupational exposure estimates for three OES have been revised in the final risk evaluation.
56, 108	**PUBLIC COMMENTS:** In the draft risk evaluation, EPA states that "distribution in commerce" "presents an unreasonable risk of injury to health (workers and ONUs)," but does not describe the analysis supporting this finding. • EPA did not prepare even a qualitative evaluation of distribution in commerce of TCE. EPA should clarify how it analyzed distribution and provide the basis for its finding of unreasonable risk. EPA states that a "quantitative evaluation of the distribution of TCE was not included in the risk evaluation because exposures and releases from distribution were considered within each condition of use"	For the purposes of the risk evaluation, distribution in commerce is the transportation associated with moving TCE in commerce. Unloading and loading activities are associated with other conditions of use. EPA assumes transportation of TCE is in compliance with existing regulations for the transportation of hazardous materials, and emissions are therefore minimal (with the exception of spills and leaks,

	• This information could not be located in the draft risk evaluation under any other COU.	which are outside the scope of the risk evaluation).
Occupational: EPA lacked or ignored workplace monitoring data; EPA should use its authority to gather monitoring data		
SACC	**SACC COMMENTS:** It is concerning that EPA did not find enough reasonably available data to determine statistical distributions for air concentrations for workers, ONUs, and consumers exposed to TCE. EPA should use its statutory authority to request studies to consider in the assessment.	EPA considered the reasonably available data and provided several opportunities for all entities to submit workplace monitoring data or other information for consideration in the risk evaluation. As noted in the document entitled EPA's Responses to Public Comments Received on the Scope Documents for the First Ten Chemicals for Risk Evaluation under TSCA (EPA-HQ-OPPT-2016-0723-0067), EPA conducted extensive and varied data gathering activities for each of the first 10 chemicals, including: • Extensive and transparent searches of public databases and sources of scientific literature, government and industry sector or other reports; • Searches of EPA TSCA 8(e), Chemical Data Reporting, and other EPA information holdings; and CBI submission holdings; • Outreach meetings with chemical manufacturers, processors, chemical users, non-governmental organizations, trade organizations, and other experts, including other State and Federal Agencies (*e.g.,* Dept of Defense, NASA, OSHA, NIOSH, FDA and CPSC); and • Publication of conditions of use documents, scope documents, and problem formulation
100	**PUBLIC COMMENTS:** EPA has ready access to a wealth of occupational exposure data and the ability to require the production of that data under TSCA. No effort was made to review that data when preparing the draft risk evaluation. For several COUs, EPA did not seek or receive any monitoring data, relying instead on modeling or unsupported extrapolations from other uses of TCE. • For the use of TCE in spot cleaning, EPA estimates that up to 269,000 workers per year are exposed in up to 63,748 facilities, yet the draft risk evaluation considered only eight data points to estimate such exposures. EPA's failure to identify relevant monitoring data does not mean that such data do not exist.	
108	**PUBLIC COMMENTS:** When a data gap exists, EPA cannot rationally assume that the absence of evidence regarding a particular hazard or exposure establishes that the hazard or exposure is not present. Such assumptions violate EPA's duty to consider all reasonably available information, which EPA could generate to fill these data gaps, as well as EPA's duty to use the best available science.	

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		documents to solicit information generally from industry, nongovernmental organizations, and the public.
108	**PUBLIC COMMENTS:** For numerous COUs, EPA lacked adequate monitoring data.	EPA considered the reasonably available data and provided several opportunities for all entities to submit workplace monitoring data or other information for consideration in the risk evaluation.
SACC, 56, 108, 100	**SACC COMMENTS:** EPA does not use the wealth of OSHA data because it may not be representative (potential for bias). These OSHA data are unlikely to be any less representative than using monitoring results from a single plant with a small number of measurements as is used for the exposure derivation in this draft risk evaluation. **PUBLIC COMMENTS:** EPA appears to have ignored OSHA data and dismisses it as "biased." EPA only relied on OSHA data for a single COU (metalworking fluids, 3 data points) and incorporated OSHA data into an additional two COUs (adhesives, sealants, paints, and coatings as well as spot cleaning and wipe cleaning, <8 data points) despite OSHA having 3,225 air samples for TCE. • There is a substantial amount of TCE exposure data from OSHA inspections available online; however, EPA failed to consider the majority of that data in its draft risk evaluation. • It is unclear why the other OSHA data – which are not even mentioned in the systematic review supplemental file on environmental releases and occupational exposure – have not been incorporated. EPA must acquire all of the relevant OSHA data on TCE in order to comply with its requirements to consider reasonably available information and the best available science, in accordance with TSCA. • EPA's decision to highlight potential bias in OSHA data is	EPA used the highest quality data reasonably available for all scenarios, including OSHA data. EPA consulted with and obtained data from OSHA, whose data are used and cited in the Risk Evaluation as (OSHA, 2017). EPA consults regularly with its federal partners and will consult with state agencies if they are known to have relevant occupational exposure data. EPA's discussions and consultation with OSHA are described in section 1.4.5.2 of Supplemental Information on Releases and Occupational Exposure Assessment. Additionally, EPA conferred with OSHA and NIOSH during interagency review and their contributions during review are reflected in the Draft and Final Risk Evaluation. EPA regularly engages with OSHA along with its other federal partners. However, it should be noted that under section 6 of TSCA, EPA is not mandated to consult with OSHA. Under section 9(a) of TSCA, the Administrator may determine

	unjustified and likely inaccurate.	it is appropriate, after making an unreasonable risk finding, to refer an action to OSHA, but the Agency is not mandated to do so. Regarding monitoring data from state agencies and industry, EPA has considered the reasonably available data, including from states, and has provided several opportunities for all entities to submit workplace monitoring data or other information for consideration in the risk evaluation. EPA engages with all its federal partners as it works to conduct and refine its risk evaluations. EPA is under no obligation to categorically provide descriptions of its discussions and consultations with other federal agencies and, in the interest of continuing to have open and candid discussions with them, is not intending to include the content of those discussions in the risk evaluation. However, input from federal partners is included as appropriate.
108	**PUBLIC COMMENTS:** During the SACC meeting, several reviewers questioned EPA's sparse use of the OSHA data and EPA's assertion that such data are not representative. One peer reviewer questioned whether the OSHA data are at least as representative as the single-site Halogenated Solvents Industry Alliance (HSIA) data that EPA used. It was suggested that EPA consider a composite data analysis – combining the OSHA data and the HSIA data – to increase the confidence compared to relying on data from a single study/site.	EPA used the highest quality data reasonably available for all scenarios, including OSHA data. EPA consulted with and obtained data from OSHA, whose data are used and cited in the Risk Evaluation as (OSHA, 2017). EPA consults regularly with its federal partners and will consult with state agencies if they are known to have relevant occupational exposure data. EPA's discussions and consultation with OSHA are described in section 1.4.5.2 of

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		Supplemental Information on Releases and Occupational Exposure Assessment. Additionally, EPA conferred with OSHA and NIOSH during interagency review and their contributions during review are reflected in the Draft and Final Risk Evaluation. EPA regularly engages with OSHA along with its other federal partners. However, it should be noted that under section 6 of TSCA, EPA is not mandated to consult with OSHA. Under section 9(a) of TSCA, the Administrator may determine it is appropriate, after making an unreasonable risk finding, to refer an action to OSHA, but the Agency is not mandated to do so. Regarding monitoring data from state agencies and industry, EPA has considered the reasonably available data, including from states, and has provided several opportunities for all entities to submit workplace monitoring data or other information for consideration in the risk evaluation. EPA engages with all its federal partners as it works to conduct and refine its risk evaluations. EPA is under no obligation to categorically provide descriptions of its discussions and consultations with other federal agencies and, in the interest of continuing to have open and candid discussions with them, is not intending to include the content of those discussions in the risk evaluation. However, input from federal partners is included as appropriate.

100	**PUBLIC COMMENTS:** • OSHA requires employers to preserve and maintain employee exposure records including "the sampling results, the collection methodology (sampling plan), a description of the analytical and mathematical methods used, and a summary of other background data relevant to interpretation of the results obtained" for 30 years. • OSHA's respirator standard also requires that employers "evaluate the respiratory hazards at their workplaces," including a quantitative determination of potential exposures so the employer can determine whether respirators are required and, if so, what type of respirator will adequately protect workers. Therefore, employers would have significant amounts of workplace exposure data that would be reasonably available to EPA. If no such data exist, then assumptions of widespread and health-protective respirator use are wrong.	EPA used the highest quality data reasonably available for all scenarios, including OSHA data. EPA consulted with and obtained data from OSHA, whose data are used and cited in the Risk Evaluation as (OSHA, 2017). EPA assumes for some conditions of use, the use of appropriate respirators is not a standard practice, based on best professional judgment given the burden associated with the use of supplied-air respirators, including the expense of the equipment, and the necessity of fit-testing and training for proper use. The risk evaluation also presents estimated risk in the absence of PPE and does not assume that occupational non-users use PPE.
108, 100	**PUBLIC COMMENTS:** In response to previous comments EPA acknowledged its duty to consider "reasonably available information" and while EPA details its "data gathering activities," EPA has not established that these activities will result in EPA obtaining all of the reasonably available information that EPA could "generate, obtain, and synthesize" if EPA also used its authorities under TSCA to obtain additional information. • Thus, EPA has not established that it will obtain all reasonably available information. EPA appears to recognize that voluntary requests standing alone are insufficient. Despite that acknowledgement, EPA still has not relied on its available authorities to obtain additional information. • A voluntary call is much less likely to produce all of the necessary information than rules mandating that affected parties provide the requested information. • EPA has provided no empirical evidence establishing that this	As noted in the document entitled EPA's Responses to Public Comments Received on the Scope Documents for the First Ten Chemicals for Risk Evaluation under TSCA (EPA-HQ-OPPT-2016-0723-0067), EPA conducted extensive and varied data gathering activities for each of the first 10 chemicals, including: • Extensive and transparent searches of public databases and sources of scientific literature, government and industry sector or other reports; • Searches of EPA TSCA 8(e), Chemical Data Reporting, and other EPA information holdings; and CBI submission holdings;

	voluntary approach will result in EPA obtaining all "reasonably available" information. • Manufacturers and processors of TCE have a vested interest in EPA finding that TCE does not present an unreasonable risk. It raises concern that companies by choose to "cherry pick" information, or not voluntarily provide information at all. • Because of this reality and appearance of partiality, relying solely on voluntary measures decreases the credibility of this risk evaluation. If EPA acts under TSCA, the regulations impose some requirements that will help ensure the accuracy and completeness of the information. To the extent that it relies on voluntary submissions from industry, EPA needs to take additional steps to better ensure that the voluntary information it receives is accurate and complete. EPA would need to develop a more rigorous and structured process. For example, EPA's submission process does not appear to require anyone to certify that the information in their submissions is accurate or complete to the best of their knowledge. EPA should consider approaches for vetting statements and assertions, particularly when made by entities with a financial interest in the outcome of these risk evaluations.	• Searches for Safety Data Sheets (SDSs) using the internet, EPA Chemical and Product Categories (CPCat) data, the National Institute for Health's (NIH) Household Product Database, and other resources in which SDS could be found; • Preparation of a market analysis using proprietary databases and repositories; • Outreach meetings with chemical manufacturers, processors, chemical users, non-governmental organizations, trade organizations, and other experts, including other State and Federal Agencies (*e.g.,* Dept of Defense, NASA, OSHA, NIOSH, FDA and CPSC); and • Publication of conditions of use documents, scope documents, and problem formulation documents to solicit information generally from industry, nongovernmental organizations, and the public. EPA requested information on all aspects of risk evaluations throughout the risk evaluation process, including opening public dockets for receipt of such information, conducting outreach to manufacturers, processors, users and other stakeholders, as well as conducting tailored data development efforts for some of the first 10 chemicals. Given the timeframe for conducting risk evaluations on the first 10 chemicals, use of TSCA data gathering authorities has been limited in scope.

		EPA had sufficient information to complete the TCE risk evaluation using a weight of scientific evidence approach. EPA selected the first 10 chemicals for risk evaluation based in part on its assessment that these chemicals could be assessed without the need for regulatory information collection or development. When preparing this risk evaluation, EPA obtained and considered reasonably available information, defined as information that EPA possesses, or can reasonably obtain and synthesize for use in risk evaluations, considering the deadlines for completing the evaluation. However, EPA will continue to improve on its method and data collection for the next round of chemicals to be assessed under TSCA. All studies used in the Risk Evaluation, including industry submissions, are evaluated using the same data quality criteria under the TSCA Systematic Review process described in the document, Application of Systematic Review in TSCA Risk Evaluations. In consideration of comments received, EPA is in the process of updating the TSCA Systematic Review protocol to improve the transparency of this review process and further reduce possible bias such that all studies are appropriately considered. EPA identifies the uncertainty of representativeness as a primary uncertainty for each occupational exposure scenario that

		includes monitoring data. The Uncertainties section 4.3.2.1 provides detailed discussion of this potential bias and notes that limited data sets may potentially underestimate or overestimate exposures. EPA describes data quality ratings in its *Application of Systematic Review in TSCA Risk Evaluations*.
Occupational: Additional worker monitoring data for EPA to consider		
97	**PUBLIC COMMENTS:** EPA's preliminary conclusion was based upon a significant over-estimation of the level of exposure for workers and ONUs to TCE when processed as a reactant/intermediate in industrial gas manufacturing. • Additional industrial hygiene and emission monitoring data is provided by the commenter that demonstrates exposure to TCE use as a refrigerant feedstock is *de minimus* and does not pose an unreasonable risk of injury to human health (workers and ONUs). • This new information should be adequate for EPA to conclude that processing TCE as a reactant/intermediate in industrial gas manufacturing (*e.g.,* manufacture of fluorinated gases used as refrigerants, foam blowing agents and solvents) does not present an unreasonable risk of injury to health workers and ONUs.	Inhalation monitoring data from manufacturing facilities were used as surrogate for other conditions of use. This data was chosen as TCE concentrations for these conditions of use would be similar to manufacturing, and TCE exposures during unloading would be comparable in magnitude to TCE loading following manufacture. Following publication of the draft risk evaluation, one industry stakeholder that uses TCE as a feedstock in the manufacture of refrigerants provided occupational exposure information which was added to the manufacturing data. As a result, occupational exposure estimates for three OES have been revised in the final risk evaluation.
Occupational: EPA's reliance on occupational exposure data from HSIA is invalid		
SACC	**SACC COMMENTS:** Recommendation: Discuss the implications of using monitoring data from surrogate scenarios that can differ in the level and extent of exposure controls. • EPA should discuss that HSIA data could be under better controlled exposures compared to scenarios in other categories.	HSIA data were provided as part of continuous IH monitoring programs and were evaluated using the same criteria as all other data sets. Following publication of the draft risk

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	• The link to the HSIA data in the draft risk evaluation is incorrect; it is not to the exposure monitoring data.	evaluation, one industry stakeholder that uses TCE as a feedstock in the manufacture of refrigerants provided occupational exposure information which was added to the manufacturing data. As a result, occupational exposure estimates for three OES have been revised in the final risk evaluation. The ranking of data sources in the Risk Evaluation is reflective of the approaches outlined in *Application of Systematic Review in TSCA Risk Evaluations.* EPA is in the process of seeking peer review of its Systematic Review protocol, and potential bias of data sources may be addressed in future updates. EPA used the highest quality data reasonably available for all scenarios, and the combined HSIA and industry-supplied data are the highest quality data for three COUs. Independent validation of data is not available for these COUs.
56, 108, 100	**PUBLIC COMMENTS:** EPA inappropriately relies solely on occupational exposure data from the HSIA for three COUs, "Manufacturing," "Processing as a Reactant," and "Other Industrial Uses." HSIA is the main trade association for manufacturers of TCE, and, as such, it has a strong vested interest in EPA finding the chemical present as low a risk as possible. This vested interest calls into question the reliability and completeness of the data voluntarily submitted by HSIA. There is concern over EPA's reliance on voluntarily submitted industry data. EPA made some questionable decisions regarding HSIA data. • During systematic review, EPA assigned the data a score of "1" for Geographic Scope because the data come from U.S. facilities. However, the data represent only one manufacturing facility, which	HSIA data were provided as part of continuous IH monitoring programs and were evaluated using the same criteria as all other data sets. Following publication of the draft risk evaluation, one industry stakeholder that uses TCE as a feedstock in the manufacture of refrigerants provided occupational exposure information which was added to the manufacturing data. As a result, occupational exposure estimates for three OES have been revised in the final risk evaluation.

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	is unlikely to be representative of the entire country. • EPA scored the HSIA data a "1" for "Sample Size," even though the dataset is only comprised of 16 samples. • EPA assigned the 2018 data a "3" for Methodology explaining that "no method provided by the HSIA Industry organization." However, EPA's approach to weighting criteria, which is inconsistent with best practices in systematic reviews, results in the "Low" Methodology score having little impact on the overall score. • EPA fails to acknowledge potential bias and provides insufficient justification for its exclusive reliance this data without independent validation and quality assurance reporting. • EPA has not adequately compared HSIA's data to that available through OSHA.	The ranking of data sources in the Risk Evaluation is reflective of the approaches outlined in *Application of Systematic Review in TSCA Risk Evaluations.* EPA is in the process of seeking peer review of its Systematic Review protocol, and potential bias of data sources may be addressed in future updates. EPA used the highest quality data reasonably available for all scenarios, and the combined HSIA and industry-supplied data are the highest quality data for three COUs. Independent validation of data is not available for these COUs.
100	**PUBLIC COMMENTS:** EPA used HSIA manufacturing data as a surrogate to estimate occupational exposures from the processing of TCE as a reactant and for other industrial uses of TCE, despite acknowledging that EPA is "unsure of the representativeness of these surrogate data toward actual exposures to TCE." • HSIA's data cover 16 data points from a single manufacturing facility, from which EPA extrapolates exposures for up to 500 facilities nationwide that manufacture TCE, process it as a reactant, or use it in other industrial operations. • EPA identifies no reason to believe that this sparse data set, is representative of the industry as a whole. • Moreover, HSIA did not provide any information about the conditions under which these samples were taken or the sampling protocols and methodology. EPA relied on the HSIA data without questioning its reliability or representativeness.	HSIA data were provided as part of continuous IH monitoring programs and were evaluated using the same criteria as all other data sets. Following publication of the draft risk evaluation, one industry stakeholder that uses TCE as a feedstock in the manufacture of refrigerants provided occupational exposure information which was added to the manufacturing data. As a result, occupational exposure estimates for three OES have been revised in the final risk evaluation. The ranking of data sources in the Risk Evaluation is reflective of the approaches outlined in *Application of Systematic Review in TSCA Risk Evaluations.* EPA is in the process of seeking peer review of its Systematic Review protocol, and potential bias of data sources may

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		be addressed in future updates. EPA used the highest quality data reasonably available for all scenarios, and the combined HSIA and industry-supplied data are the highest quality data for three COUs. Independent validation of data is not available for these COUs.
Occupational: Comments on EPA's approaches and use of monitoring or modeled data for exposure assessment		
SACC	**SACC COMMENTS:** Recommendation: Explore statistical and computational approaches to better utilize available monitoring data and produce more representative exposure estimates. The Committee suggested that EPA identify the drivers for model exposure estimates (from the Monte Carlo simulations), and how changing values in these drivers affect differentially the central tendency and high-end model-based exposure estimates in comparison to estimates based on measurements. This exercise could provide insights into the assumptions that need refinement or improved data. • Statistical and computational approaches (such as censored estimation, Bayesian methods, and Monte Carlo simulation; see for example Helsel, 2005; Gelman et al., 2004; and Robert and Casella, 2004) can be used to derive better estimates of exposure statistics (means, medians, variances, interquartile ranges, minimums, and maximums) from unknown distributions. EPA should use these techniques in evaluations to overcome limitations in available monitoring data. The alternative is to use TSCA statutory authority to mandate and/or implement adequate monitoring programs to fill this data need.	EPA thanks the commenter for the recommendation. EPA will investigate methods to apply to monitoring data, which may include statistical and computational approaches, for future risk evaluations.
SACC	**SACC COMMENTS:** Monitoring data are not intended to accurately reflect the range of worker exposures across an industry or a COU and unlikely to account for the full range of variability of OESs. Typically, too few workers are monitored, it is done over a short period of time, and collected at only one or a few sites. Data and associated statistics are likely biased and	EPA used the highest quality data reasonably available for all scenarios, including monitoring data. Monitoring data is at the top of the hierarchy of approaches for occupational exposure assessments. EPA will seek peer

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	there is differential reliability between sets of samples. These are unlikely true estimates of central tendency.	review of its Systematic Review protocol, including the hierarchy of approaches to exposure estimation.
SACC	**SACC COMMENTS:** TSCA evaluations should be using a composite approach to understanding exposure. The draft risk evaluation uses summary central tendency and high-end descriptors, so compiling all of the data would provide a broader base.	EPA considered the reasonably available information and used the best available science to determine whether to consider aggregate exposures for a particular chemical. EPA has determined that using the high-end risk estimate for inhalation and dermal risks separately as the basis for the unreasonable risk determination is a best available science approach. There is low confidence in the result of aggregating the dermal and inhalation risks for this chemical if EPA uses an additive approach, due to the uncertainty in the data. EPA will seek peer review of its Systematic Review protocol, including the hierarchy of approaches to exposure estimation.
50	**PUBLIC COMMENTS:** In several cases, (batch open-top vapor degreasing, conveyorized vapor degreasing, metalworking fluids, spot cleaning and wipe cleaning, and other commercial uses), EPA presents both monitoring and modeled data for inhalation exposures to workers. EPA states, "If both, inhalation monitoring data and exposure models were reasonably available, where applicable, EPA presented central tendency and high-end exposures using both." • The SACC should consider whether EPA's justification of which OESs warranted both monitoring and modeling approaches is sufficient, and whether EPA has adequately detailed the circumstances and process for determining which of these approaches is ultimately used for risk characterization.	EPA presented two sets of inhalation estimates only where both inhalation monitoring data and exposure models were reasonably available. Presenting both estimates allowed comparability between the data sets. EPA will seek peer review of its Systematic Review protocol, including the presentation of exposures based on both monitoring and modeling.

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SACC	**SACC COMMENTS:** This Evaluation, as others previously reviewed by the SACC, uses the Nicas (2009) two-zone box model for estimating occupational inhalation exposures. The Committee recommended that EPA explore other models available in the research literature for estimating vapor generation.	EPA thanks the commenter for the recommendation. EPA will investigate whether alternative methods to estimate vapor generation are appropriate for future risk evaluations.
103	**PUBLIC COMMENTS:** EPA should use a tiered approach to assessing exposure. By beginning with screening-level assessments that rely on health-protective assumptions to estimate exposure values, the resulting risk calculations will not underestimate risks but will likely overestimate them. This will allow EPA to recognize COUs with no unreasonable risk quickly and set these aside as not needing further evaluation. Substances identified by screening-level analyses as needing additional attention would then proceed to the next analytical tier using a more sophisticated model. These higher tiered exposure models are designed to provide more accurate exposure estimates, so that the higher tiered risk evaluation of such substances will yield more precise risk estimates.	EPA thanks the commenter for the recommendation. EPA will investigate whether a tiered exposure approach can be utilized to assess exposure for future risk evaluations.
103	**PUBLIC COMMENTS:** Future risk evaluations should provide guidance on how EPA plans to choose between modeled data and monitored data. The TCE risk evaluation featured five COUs that had both monitoring and modeled data and these data were largely congruent, but that may not be the case in other evaluations. Additional clarity regarding what data constitutes "reasonable availability" would be instructive, particularly if that involves non-trivial Monte Carlo simulations.	EPA has included the hierarchy of approaches in Section 2.3.1.2 of the Risk Evaluation. This section shows the hierarchy has preferences, and these preferences do not have to be strictly followed. EPA will seek peer review of its Systematic Review protocol, including the hierarchy of approaches to exposure estimation.
Occupational: Assumptions EPA used for exposure estimates for specific COUs are invalid		
100	**PUBLIC COMMENTS:** EPA estimates TCE exposures from metalworking fluids based on the expected concentrations in the mist created by the use of such fluids. EPA acknowledges that "these estimates may underestimate exposures to TCE during use of metalworking fluids as they do not account for exposure to TCE that evaporates from the mist droplets into the air." • EPA does not attempt to quantify or correct for this underestimation;	EPA stated this potential exposure underestimate as an uncertainty. Risk was determined for this OES using this modeling approach. EPA thanks the commenter for the information concerning NIOSH's methodology for sampling and analysis. EPA consults regularly with its federal

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	instead, it says that "[t]his exposure is difficult to estimate and is not considered in this assessment." The fact that realistic exposure scenarios may be more "difficult" or less "certain" to estimate does not permit EPA to rely on inaccurate exposure assumptions that understate worker risks. • NIOSH has recommended a methodology for the sampling and analysis of metalworking fluid aerosols (mist). • The draft risk evaluation must account for metalworkers' TCE inhalation from evaporated mists.	partners and will consult with NIOSH on this topic for future risk evaluations.
108	**PUBLIC COMMENTS:** EPA's analysis of distribution was inadequate in the draft risk evaluation. EPA stated that: "Activities related to distribution (*e.g.,* loading and unloading) will be considered throughout the TCE life cycle, rather than using a single distribution scenario." • EPA assumes exposure from distribution occurs only during loading and unloading. It is not clear how, if at all, EPA considered exposures from loading and unloading under individual COUs, as it presents no specific analysis of these activities in the context of the various COUs. • EPA does not appear to address exposures from distribution aside from those arising from loading and unloading. Does EPA assume that all distribution occurs through "closed systems" which lead to no releases or exposure? • EPA provides no evidence or support for any assumption that TCE is always distributed in closed systems leading to no releases or exposures. EPA has provided no evidence that exposures and releases during distribution will be nonexistent.	For the purposes of the risk evaluation, distribution in commerce is the transportation associated with moving TCE in commerce. Unloading and loading activities are associated with other conditions of use as discussed in the Supplemental Information File: Environmental Releases and Occupational Exposure Assessment. EPA assumes transportation of TCE is in compliance with existing regulations for the transportation of hazardous materials, and emissions are therefore minimal (with the exception of spills and leaks, which are outside the scope of the risk evaluation).
Occupational: EPA must identify all occupational exposure pathways		
SACC	**SACC COMMENTS:** Recommendation: Specifically identify all occupational exposure pathways with their associated regulatory authority. The draft risk evaluation should address more specifically those occupational exposure pathways that are not included because of	EPA provides a list of previous TCE assessments in Table 1-2 and TCE's regulatory history is covered in Appendix A. Exposure pathways addressed by other EPA-administered

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	competing areas of regulatory mandate. For example, lace wig and hair extension glues are excluded because they are considered cosmetics (Food and Drug Administration [FDA] regulation), but hoof polish, used for cosmetic purposes and not considered a veterinary medicine under FDA regulations, remains under TSCA. A table should be included that specifically lists all the excluded pathways, and which indicates whether risk assessments are available for these pathways from other regulatory programs.	statutes are discussed in detail in Section 1.4.2. Section 1.4.2 has been added to the final risk evaluation in response to these and other SACC and public comments.
SACC	**SACC COMMENTS:** Recommendation: Provide a rationale for not estimating the separate vapor and particle-bound fractions of TCE-containing aerosols in the near field. It is not clear whether the literature on liquid aerosol modeling has been examined to see if it would be possible to estimate the vapor phase/particle-bound fraction of TCE in aerosols generated in close proximity to the worker applying the product. Despite the rapid volatilization of TCE from droplets, it is likely that a sizable portion of the TCE is in the particle-bound phase close to the worker, not completely in the vapor phase.	In each case where EPA models inhalation exposures using the NF/FF model, this exposure is the combined inhalation exposure to vapor and particulates. The aerosol degreasing model is the one exception. This model assumes that an aerosol is formed when sprayed from the can. The droplets may evaporate TCE vapors into the air. Also, the degreaser droplets may hit the brake surface, and some may adhere to the tool the worker uses to scrape the brake. But EPA assesses that all such TCE is ultimately released into the air (and does so rather quickly) such that the worker is exposed to the airborne concentration formed by the total mass of TCE released from the aerosol can. This is a more protective assumption.
Occupational: EPA's reliance/assumptions about OSHA's Permissible Exposure Limit (PEL) is invalid		
56, 108, 61, 100	**PUBLIC COMMENTS:** It is inappropriate for EPA to assume that there is compliance with OSHA's PEL and that it would be health protective. • The data indicate exactly the opposite of what EPA assumes: the existence of real-world exposure monitoring data above the PEL demonstrate that non-compliance is both known to occur and is	EPA did not exclude data if it exceeded the OSHA PEL. Some data were excluded based on finding the study/data source as unacceptable. EPA has outlined specific criteria for identifying a study as unacceptable in *Application of*

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	reasonably foreseeable. • The OSHA PEL, set at 100 ppm, was adopted in 1971, and is outdated and inadequate for ensuring protection of worker health. OSHA acknowledged that "studies have indicated that chronic exposure to less than 100 ppm TCE is associated with a variety of nervous disturbances," and EPA found that developmental TCE exposure is associated with fetal cardiac malformations at concentrations less of than 1 ppm, and a range of other unreasonable risks at concentrations less than 10 ppm. • EPA has previously recommended the use of the 2 ppm NIOSH Recommended Exposure Limit (REL). • EPA also developed a recommendation for an Existing Chemical Concentration Limit, or "ECEL" of 1 ppb (8-hour time weighted average) as a more current benchmark for workplace exposures. • However, under the assumption of compliance, in its "PEL-capped" analysis, EPA ignored/excluded real-world workplace monitoring data that are above 100 ppm. It is inappropriate for EPA to consider excluding data points collected in the real world on the basis of its flawed assumption of universal compliance with regulatory requirements. EPA must utilize the full dataset, regardless of whether data points are above or below the PEL.	*Systematic Review in TSCA Risk Evaluations*. For the single OES in which modeled exposure estimates were above the PEL (Batch Open Top Vapor Degreasing) EPA also presented exposures and risks based only on estimates below the PEL. For this OES, risks were identified whether exposure estimates above the PEL are excluded or not. EPA will seek peer review of its Systematic Review protocol, including the hierarchy of approaches to exposure estimation.
61	**PUBLIC COMMENTS:** The OSHA standard for TCE consists only of the PEL; it is not a comprehensive standard. OSHA's TCE standard does not require application of the hierarchy of controls, or the use of PPE, or any sort of training or education, or medical monitoring.	EPA thanks the commenter for the information.
80	**PUBLIC COMMENTS:** In 2009, the Cal/OSHA Health Effects Advisory Committee recommended that the PEL for TCE be lowered from 25 to 0.4 ppm. Since that time, EPA, the National Toxicology Program (NTP), and the International Agency for Research on Cancer (IARC) have classified TCE as a human carcinogen and based on the IRIS review in 2011, Cal/OSHA has lowered its recommended PEL for TCE to 0.2 ppm.	

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100	**PUBLIC COMMENTS:** While employers have a statutory duty to continue to protect workers against "recognized hazards" at exposures below the PEL, OSHA will cite an employer for a violation of the general duty clause only when such exposures have resulted in actual injuries or illnesses to workers. OSHA has never issued a citation to an employer under the general duty clause for TCE exposures below the PEL. • NIOSH currently recommends an exposure limit of 25 ppm over a 10-hour period, and the American Conference of Government Industrial Hygienists (ACGIH) recommends an 8-hour limit of 10 ppm.	EPA acknowledges that the OSHA regulations at 29 CFR 1910.132 require employers to assess a workplace to determine if hazards are present or likely to be present which necessitate the use of personal protective equipment (PPE). If the employer determines hazards are present or likely to be present, the employer must select the types of PPE that will protect against the identified hazards, require employees to use that PPE, communicate the selection decisions to each affected employee, and select PPE that properly fits each affected employee. EPA thanks the commenter for the information from NIOSH and ACGIH.
Dermal exposure assumptions are not valid; impact of assumptions on exposure estimates		
SACC	**SACC COMMENTS:** The dermal exposure estimates are valid or at least reasonable as a means of calculating potential dermal exposure. The mean surface areas are as described in the Exposure Factors Handbook (U.S.EPA, 2011), which uses data from the National Health and Nutrition Examination Survey (NHANES). Body weight data from NHANES can be used to construct a distribution of dermal surface areas for each age category in addition to central tendency values.	EPA thanks the commenter regarding the validity of EPA's dermal exposure estimation methods.
SACC	**SACC COMMENTS:** Recommendation: Discuss all parameters that drive all human exposure estimates based on modeling. The Committee recommended that EPA provide a clear, specific discussion about the parameters involved in calculating exposure estimates based on modeling (dermal parameters recommended by the SACC for inclusion in the current and future TSCA risk evaluations are provided in Table 6 of the SACC report) and further consider a limited	EPA conducted a sensitivity analysis for each model to evaluate how the input parameters affect modeling results. The default value and assumptions associated with each input parameter is explained in detail in the Supplemental File: TCE Environmental Releases and Occupational Exposure Assessment, which

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	sensitivity analysis to identify those parameters that most influence (drive) the exposure estimates.	was published along with the Draft Risk Evaluation.
SACC	**SACC COMMENTS:** Recommendation: Consider the potential for dermal exposure to TCE vapor. At a minimum, there should be mention and discussion of the vapor through the skin pathway of exposure, including the potential for vapor penetration through non-impermeable clothing.	An analysis in Section 2.5.1 of the Problem Formulation of the Risk Evaluation for TCE shows that absorption of TCE via skin to be orders of magnitude lower than via inhalation and that additional coverage of this topic is not included in the Risk Evaluation for TCE. EPA included expanded discussion in 2.3.1.2.5 about the f_{abs} parameter that accounts for volatilization in the estimates of dermal exposure to occupational users.
56, 108, 100	**PUBLIC COMMENTS:** EPA failed to explain or justify its assumption of one dermal exposure event per day for workers. • In an 8-hour workday, it is likely that workers would regularly engage in activities that could result in multiple exposure events per day. • In prior risk evaluations, EPA has acknowledged that this assumption "likely underestimates exposure as workers often come into repeat contact with [the same chemicals] throughout their work day," but has chosen not to consider those risks in this draft risk evaluation. EPA fails to acknowledge that this assumption will underestimate exposure. EPA has not, but must, account for this underestimation and at a minimum provide an uncertainty analysis.	EPA did not identify reasonably available information on how many contact events may occur and the time between contact events. Therefore, EPA assumes a single contact event per day for estimating dermal exposures. EPA has described events per day (FT) as a primary uncertainty for dermal modeling in the discussion of occupational dermal uncertainties section 2.3.1.3.4 as well as in the Supplemental File: TCE Environmental Releases and Occupational Exposure Assessment.
SACC	**SACC COMMENTS:** Recommendation: Provide a justification for the assumption that 10% of the skin surface will be exposed for consumer product users.	The products with impeded evaporation that were originally modeled using a surface area corresponding to 10% of hands have been updated in the final risk evaluation to consider a dermal contact area for the inside of one hand to account for the entire hand surface being in

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		contact with a rag during cleaning/degreasing activities. These products now use the same surface area assumption as the liquid formulations with impeded dermal contact.
94, 103	**PUBLIC COMMENTS:** Both occluded and non-occluded dermal TCE exposure estimates were likely to be considerably overestimated based on numerous factors, including (but not limited to): • The absorption factor for non-occluded scenarios used (8-13%), which is higher than expected under realistic scenarios, • Lack of consideration for saturation of the stratum corneum. • The assumption that the skin surface area that comes in contact with TCE is one to two full hands, rather than the more likely interior hand surfaces, • The assumption that TCE exposure occurs continuously for 8 hours rather than short intermittent exposures; and • The assumption that the worker does not change gloves or wash hands at all during the work shift. In the case of the occluded scenarios, additional overestimation likely occurred based on the assumption that the whole hand (or hands) were coated with TCE in-glove, and the lack of consideration for possible permeation back out of the glove and evaporative losses. EPA should include discussion of the impacts of these assumptions on the level of confidence in the overall estimates, and the degree to which the assumptions are more than adequately protective.	The uncertainties and limitations of the dermal modeling approach are discussed in Appendix H the Supplemental Information on Releases and Occupational Exposure Assessment document. See further discussion on occlusion in Appendix H of the Supplemental File: TCE Environmental Releases and Occupational Exposure Assessment. The occluded scenarios were presented as a what-if scenario. EPA does not know the likelihood or frequency of these scenarios in the workplace; therefore, EPA did not present risk estimates associated with occluded exposure in the Risk Evaluation.
SACC	**SACC COMMENTS:** The assumed percutaneous absorption of 100% is too high. Twenty to thirty percent would be a high estimate. Some Committee members considered the assumption of keeping TCE in contact with the skin under occluded conditions for an extended period as not a realistic exposure scenario. One Committee member pointed out that this might happen if a consumer were using a TCE-containing product without gloves and a product-soaked rag.	The uncertainties and limitations of the dermal modeling approach are discussed in Appendix H the Supplemental Information on Releases and Occupational Exposure Assessment document. See further discussion on occlusion in Appendix H of the Supplemental File: TCE Environmental

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103, 94	**PUBLIC COMMENTS:** For occluded exposure scenarios, while some chemical may splash and spill over the cuff of the glove or permeate through the glove itself over time, it is unlikely that the TCE would cover the full hand surface. A more reasonable estimate for surface area of contact would be just the palm or some fraction of the palm and fingers, rather than the full hand surface from the wrist down. • The impact of sweat inside the glove that would lower the flux of TCE through the skin (Cherrie et al., 2004) was not considered. The contribution of evaporation to the overall dose is not clear, and would require additional calculations to quantify, outside of the application of a screening model. • Ungloved hands are washed and gloves are likely removed every few hours for breaks or to switch tasks, limiting the duration of exposure events. • The assumption that 100% of the TCE that enters the glove is absorbed neglects the potential for flux of the TCE back out of the glove via evaporation during periods of no liquid contact. Flux of the TCE into the stratum corneum does not occur instantaneously. Thus, models that assume the total applied dose is available to be absorbed would overestimate actual uptake.	Releases and Occupational Exposure Assessment. The occluded scenarios were presented as a what-if scenario. EPA does not know the likelihood or frequency of these scenarios in the workplace; therefore, EPA did not present risk estimates associated with occluded exposure in the Risk Evaluation.
108	**PUBLIC COMMENTS:** EPA should present fractional absorption and applied flux assumptions side by side.	EPA default quantities that can remain on skin are based on experimental data that were measured. EPA did not find additional reasonably available actual measurements of quantity remaining on the skin form TCE, nor were citations or data provided by the commenter. The dermal assessment generated central tendency and high-end doses using models, and the models incorporated estimates of evaporation. Central tendency estimates are less than the maximum default quantity that may

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		remain on the skin. EPA did not find reasonably available empirical data or additional modeling tools proposed by this comment to inform better absorption estimates.
94	**PUBLIC COMMENTS:** EPA's high-end assumption assumed coverage of two complete hands is overly conservative and not consistent with industrial hygiene practices for glove use.	EPA's approach for developing exposure assessments for workers is to use the reasonably available information and expert judgement. When appropriate, in the risk evaluation, EPA will use exposure scenarios both with and without engineering controls and/or PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. Again, while EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgment underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. Additionally, in consideration of the uncertainties and variabilities in PPE usage (*e.g.,* dry cleaners), EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties. EPA has also outlined its PPE assumptions in section 5.1. Further, in the final

		risk evaluation for TCE, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE.
99	**PUBLIC COMMENTS:** EPA acknowledged that estimates of dermal exposure rested on questionable assumptions and likely understate the magnitude of TCE exposure by this route. • Instead of relying on test data to quantify dermal absorption rates, EPA modeled "dermal potential dose rate based on an assumed amount of liquid on skin during one contact event per day and the steady-state fractional absorption for TCE based on a theoretical framework provided by Kasting." • The assumption of rapid volatilization of TCE after skin contact did not hold true for all worker operations, including cases of occlusion, repeated contacts, dermal immersion, or activities with a high degree of splash potential. EPA, however, did not develop alternate estimates of dermal exposure using higher levels of absorption.	EPA preferentially relies on a variety of test and analog data. In the absence of suitable test data, modeling tools may be used. Because the chemical simultaneously evaporates from and absorbs into the skin, the dermal exposure is a function of both the number of contact events per day and the time between contact events. EPA did not identify information on how many contact events may occur and the time between contact events. Therefore, EPA assumes a single contact event per day for estimating dermal exposures. EPA has described the uncertainties in the dermal modeling approach in the discussion of occupational dermal uncertainties section 2.3.1.3.4 as well as in the Supplemental File: TCE Environmental Releases and Occupational Exposure Assessment.
56, 108, 99	**PUBLIC COMMENTS:** EPA does not have any actual data on glove use and efficacy. EPA recognizes the potential for occlusion, whereby glove use can *increase* skin exposure; in both the draft risk evaluation and the Supplemental File, however, exposure estimates under occluded conditions are not actually incorporated at all into the ultimate risk estimates and risk determinations for the occupational scenarios. • When comparing Table 2-15 to Tables 4-6 through 4-27, the occluded exposure scenarios disappear from the risk estimates shown	See further discussion on occlusion in Appendix H of the Supplemental File: TCE Environmental Releases and Occupational Exposure Assessment. The occluded scenarios were presented as a what-if scenario. EPA does not know the likelihood or frequency of these scenarios in the workplace; therefore, EPA did not present risk estimates associated with

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	in the latter tables. Likewise, occluded scenarios do not appear in the Supplemental Information File: Risk Calculator for Occupational Exposures (*e.g.,* see tab "RR" in EPA's "TCE-Risk Calculator for Occupational Exposures" spreadsheet). • If EPA did incorporate occlusion into its ultimate risk estimates and determinations, it needs to be far clearer on how it did so.	occluded exposure in the Risk Evaluation.
108	**PUBLIC COMMENTS:** EPA failed to consider exposure via dermal vapor. While this may not constitute a major exposure route for TCE, EPA needs to conduct the analysis to determine whether or not it can be considered negligible.	An analysis in Section 2.5.1 of the Problem Formulation of the Risk Evaluation for TCE shows that absorption of TCE via skin to be orders of magnitude lower than via inhalation and that additional coverage of this topic is not included in the Risk Evaluation for TCE. EPA included expanded discussion in 2.3.1.2.5 about the f_{abs} parameter that accounts for volatilization in the estimates of dermal exposure to occupational users.
SACC, 108	**SACC COMMENTS:** Recommendation: Discuss skin damage from contact with TCE and how it affects skin permeability to TCE. **PUBLIC COMMENTS:** EPA relies upon data that do not account for the potential impact of skin damage. Exposure to neat TCE could cause damage to skin, especially with chronic exposures, which in turn can allow for higher dermal penetration of the compound. While human data may not be available, dermal penetration from damaged skin increases ~25x, according to one peer reviewer.	The disruption of the stratum corneum leading to increased absorption is discussed in Section 3.2.2.1. EPA used a human patch test study for deriving the permeability of neat TCE, and presumably this data captured the effects of skin damage increasing absorption in participants.
94	**PUBLIC COMMENTS:** A key weakness in the EPA approach for both occluded and non-occluded exposure scenarios is the lack of consideration of chemical irritancy and task duration. Dermal exposure to TCE, particularly in neat concentration, may result in skin irritation. Some degree of skin sensation would alert the worker to the presence of the chemical; thus, a	EPA's approach for developing exposure assessments for workers is to use the reasonably available information and expert judgement. When appropriate, in the risk evaluation, EPA will use exposure scenarios both with and

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	worker would remove their gloves, wash their hands, and replace their gloves. Moreover, general industrial hygiene and worker training would dictate removal and replacement of gloves following spillage into the glove or to comply with PPE change out schedules designed to limit breakthrough time.	without engineering controls and/or PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. Again, while EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgment underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. Additionally, in consideration of the uncertainties and variabilities in PPE usage (*e.g.,* dry cleaners), EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties. EPA has also outlined its PPE assumptions in section 5.1. Further, in the final risk evaluation for TCE, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE.
94	**PUBLIC COMMENTS:** • A number of dermal occupational scenarios in the draft risk evaluation assuming worst-case scenarios yielded estimates of unreasonable risk. However, revised scenarios with more appropriate assumptions result in substantially lower exposure estimates that may impact the risk characterizations. EPA should consider whether more refined exposure assessment is warranted for some scenarios in the	EPA's approach for developing exposure assessments for workers is to use the reasonably available information and expert judgement. When appropriate, in the risk evaluation, EPA will use exposure scenarios both with and without engineering controls and/or PPE that

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	revised risk evaluation using additional information on realistic workplace scenarios coupled with appropriate modeling. • The inputs and models utilized in the draft risk evaluation resulted in estimates of exposure, and consequently, estimates of risk, that may not reflect actual industry working conditions.	may be applicable to particular worker tasks on a case-specific basis for a given chemical. Again, while EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgment underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. Additionally, in consideration of the uncertainties and variabilities in PPE usage (*e.g.*, dry cleaners), EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties. EPA has also outlined its PPE assumptions in section 5.1. Further, in the final risk evaluation for TCE, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE.
94	**PUBLIC COMMENTS:** EPA assumptions lead to overestimation of exposure for chemical manufacturing and in processing TCE as a reactant. In the majority of the operational time, TCE would only be present in closed vessels or process equipment with no dermal contact. Small magnitude exposures during short-term tasks can occur in unit operations and maintenance activities. • EPA does incorporate the use of gloves into the risk assessment	For the purposes of determining whether or not a condition of use presents an unreasonable risk, EPA incorporates assumptions regarding PPE use based on information and judgment underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in

	approach. However, based on typical industrial hygiene practice, the use of such gloves would achieve much greater protection than the default assumptions under the scenarios described for due to vaporization of TCE from the gloves. • Only non-occluded scenarios that consider various levels of glove use were modeled. For other COUs (*e.g.,* vapor degreasing), EPA estimated exposures for occluded scenarios. Some of the principles governing the occluded scenario would apply to the dose permeating the glove in the un-occluded scenarios and, therefore, are relevant to the chemical manufacturing environment.	section 5.3. Additionally, in consideration of the uncertainties and variabilities in PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties. EPA has also outlined its PPE assumptions in section 5.1. Further, in the final risk evaluation for TCE, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE.
94	**PUBLIC COMMENTS:** In the non-occluded scenario, EPA did not account for exposure duration of industrial scenarios nor the saturation of the skin by TCE. In TCE manufacturing and use as a reactant, dermal exposures are intermittent throughout the workday (*i.e.,* 1 hour or less, 4 times per shift with sufficient time in between exposures for evaporation from, or cleaning of, skin). Revised analyses using the IHSkinPerm model (provided by the commenter), in which duration and saturation factors were appropriately considered, showed that exposure scenarios without PPE in the draft risk evaluation may have overestimated the absorption fraction of TCE by 8- to 22-fold for exposure to an ungloved hand, and the total dermal dose of TCE by 6- to 17-fold for exposure to an ungloved hand assuming four one-hour exposure events per day.	The dermal model used by EPA considers competing processes of absorption into the skin and evaporation. The model does not assume continuous exposure with liquid TCE, only that the applied dose (*i.e.,* the amount of chemical remaining on the skin after contact with the exposure source) remains on the skin until it is absorbed or evaporates. Based on the physiochemical properties of TCE, this duration may not be very long after initial contact.
Data considered for dermal exposure estimates were invalid or incomplete		
SACC	**SACC COMMENTS:** Recommendation: Estimate dermal exposure to neat liquid TCE using experimental *in vivo* human data described in Stewart and Dodd (1964); Sato and Nakajima (1978); and Kezic et al. (2001). TCE is known to cause dermatitis, which implies skin barrier damage. Data reflecting exposure to neat TCE are needed. Human data show a maximum flux exceeding the flux estimated from the Poet et al. (2000) permeability coefficient, and is consistent with the Morgan et al. (1991) rat study. Based on these data, EPA should conclude that the best	Based on comments from the SACC, EPA updated dermal permeability modeling for the final Risk Evaluation to utilize results for neat permeability from human data in Kezic et al, 2001 as opposed to data from aqueous TCE, as was used previously.

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	estimate of permeation in humans from neat exposure would be an approximation based on the results of these studies.	
108	**PUBLIC COMMENTS:** If EPA does not have sufficient information on dermal exposure whether through measured or modeled data, it should have used its authorities to obtain them.	EPA believes it had sufficient information to complete the TCE Risk Evaluation using a weight of scientific evidence approach. EPA selected the first 10 chemicals for Risk Evaluation based in part on its assessment that these chemicals could be evaluated without the need for regulatory information collection or development. When preparing this Risk Evaluation, EPA obtained and considered reasonably available information, defined as information that EPA possesses, or can reasonably obtain and synthesize for use in Risk Evaluations, considering the deadlines for completing the evaluation. 40 CFR 702.33 Given the timeframe for conducting Risk Evaluations on the first 10 chemicals, use of TSCA data gathering authorities has been limited in scope. In general, EPA intends to utilize TSCA data gathering authorities more routinely for the next 20 Risk Evaluations.
56, 108, 99	**PUBLIC COMMENTS:** EPA assumed a dermal absorption rate of 8% in industrial settings and 13% in commercial settings based on the Kasting and Miller (2006) model; however, elsewhere, EPA indicates that dermal absorption is rapid, citing other research. • It is unclear whether EPA considered this latter research when setting the fractional absorption rates of 8% and 13%. If not, the model used may underestimate dermal exposure, given the cited human and excised skin tissue studies specific to TCE. • EPA cited ATSDR (2019), which reviewed a number of studies of	There is a difference between how *fast* absorption occurs and how *much* absorption occurs. The commenter seems to be confusing these. There are competing processes of absorption and evaporation that lead to the calculated percent absorbed. For other solvents where experimentally derived percent absorption values were available, the actual absorption was lower, not greater, than the model's prediction.

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	TCE dermal absorption. EPA failed to consider those studies and their implications for assumed rates of dermal absorption. This is in violation of the requirement to base its risk determinations on all "reasonable available information" and the "best available science."	EPA used the best available science and reasonably available data to assess exposures for each COU. EPA appreciates any additional data from commenters that would improve its estimates of occupational exposures.
Dermal exposure model is incomplete; modeling improvements/additional modeling suggestions		
SACC	**SACC COMMENTS:** The Committee expressed concerns about the suitability of the permeability sub-model (P_DER2b). For consumer exposure to liquid TCE EPA selected a permeability coefficient published by Poet et al. (2000) and derived from fitting of a PBPK model. Two issues arise with respect to this modeling approach • PBPK models typically treat skin as a well-mixed compartment rather than as a membrane. Because the underlying mathematics is different, the numerical value of the coefficient can be affected (see Norman et al., 2008). • Such models represent multi-variable fitting exercises. Due to compensating errors, good fits can be achieved by poor estimates of more than one parameter. Parameter values obtained from PBPK fitting should be checked against values obtained by other means. The permeability coefficient obtained from Poet et al. (2000) does not appear unreasonable for absorption from aqueous media. However, the draft risk evaluation pairs an aqueous phase permeability coefficient with the concentration of the neat liquid. This approach is invalid. • The maximum concentration that can legitimately be paired with an aqueous-phase permeability coefficient is that of the saturation concentration in water. Barring skin damage by the pure solvent, this should result in an overestimate of the maximum flux (and hence absorbed dermal dose).	Based on comments from the SACC, EPA updated dermal permeability modeling for the final Risk Evaluation to utilize results for neat permeability from human data in (Kezic et al. 2001) as opposed to data from aqueous TCE, as was used previously.
99	**PUBLIC COMMENTS:**	

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	EPA did not model any repeat contact scenarios. EPA should model a broader range of dermal contact scenarios based on its own analysis of variations in dermal exposure conditions and base risk estimates on multiple dermal exposure events per day. It should also estimate increases in exposure and risk where occlusion results in higher skin absorption of TCE during glove use.	EPA did not identify information on how many contact events may occur and the time between contact events. Therefore, EPA assumes a single contact event per day for estimating dermal exposures. EPA has described events per day (FT) as a primary uncertainty for dermal modeling in the discussion of occupational dermal uncertainties section 2.3.1.3.4 as well as in the Supplemental File: TCE Environmental Releases and Occupational Exposure Assessment. See further discussion on occlusion in Appendix H of the Supplemental Information on Environmental Releases and Occupational Exposure Assessment document. The occluded scenarios were presented as a what-if scenario. EPA does not know the likelihood or frequency of these scenarios in the workplace; therefore, EPA did not present risk estimates associated with occluded exposure in the Risk Evaluation.
108	**PUBLIC COMMENTS:** In the problem formulation, EPA states: "EPA anticipates that existing EPA/OPPT dermal exposure models would not be suitable for quantifying dermal exposure to highly volatile chemicals such as TCE." The draft risk evaluation does not acknowledge this concern or make clear whether or how it was addressed.	Unlike the EPA/OPPT dermal model, the Dermal Exposure to Volatile Liquids Model (DEVL) model incorporates the evaporation of the material from the dermis. The DEVL model was used to estimate dermal exposures to TCE for the Risk Evaluation. More information on the DEVL model can be found in Appendix H of the Supplemental File: Environmental Releases and Occupational Exposure.
99	**PUBLIC COMMENTS:**	

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	EPA uses different dermal absorption models for consumer and workplace exposure scenarios – assuming that absorption is on the order of 8-13% for workers but 0.8% for consumers – without clearly stating the rationale. The implication that worker dermal exposure is longer in duration than consumer exposure is inconsistent with EPA's premise that both exposures involve one-time events.	Differences between occupational and consumer assessment approaches are addressed in Section 4.3.2.3. The choice of one model over the other is primarily driven by the exposure scenario that needs to be assessed and the information that is reasonably available. For example, EPA does not know the exact duration of exposure for occupational loading and unloading hence EPA used the engineering model for occupational exposure assessment since it is event based and does not require a duration input. In contrast, for consumer applications there is reasonably available information for duration of use, hence the CEM permeability model or the fraction absorbed model can be used for these exposure scenarios with greater confidence. Overall, the models are considered appropriate for their respective uses based on the reasonably available information.
94	**PUBLIC COMMENTS:** The exposure assessment for the dermal route was conducted using the DEVL model using various scenario centric parameters that are applied with little justification.	More information on the DEVL model and associated parameters can be found in Appendix H of the Supplemental File: Environmental Releases and Occupational Exposure.
94	**PUBLIC COMMENTS:** • EPA's approach of assuming all occluded doses cannot be corrected using IHSkinPerm. In IHSkinPerm, the thickness of the air layer would have to be greatly increased (towards infinity) or the vapor pressure of TCE would have to be greatly decreased (towards 0) to correctly simulate, assuming no ability for TCE to escape the occluded environment. • Exposure duration becomes even more important for occluded contact, and a flux-based model assuming that no or negligible	The draft risk evaluation excluded dermal consumer exposure scenarios without impeded evaporation. Dermal approaches were revised for the final draft with additional evaluation incorporated for whether the condition of use was expected to have expectation of impeded vs. unimpeded dermal evaporation. For those scenarios expecting impeded dermal

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	evaporation is recommended as a conservative estimate. IHSkinPerm is difficult to modify to account for negligible evaporation.	evaporation, EPA utilized the Permeability submodel within CEM and for those expecting unimpeded dermal evaporation, EPA utilized the Fraction absorbed submodel within CEM. This has been explained more fully within Section 2.3.2.4.1. EPA presents the results for the model deemed to be most appropriate (permeability for impeded evaporation, fraction absorbed for unimpeded evaporation) within the Risk Evaluation, however results via both methods are provided for all COUs in the Supplemental File *Exposure Modeling Results and Risk Estimates for Consumer Dermal Exposures*. EPA has provided a discussion of key sources of uncertainty for occupational dermal scenarios in section 2.3.1.3.4. EPA may explore the range of possible exposures utilizing different models in future assessments.
99	**PUBLIC COMMENTS:** EPA failed to include dermal exposure in risk determinations for several consumer products. EPA's claim that it can dismiss dermal exposure because it is *de minimis*, or unlikely to contribute significantly to overall exposure, is not consistent with realistic use scenarios for these products and in conflict with how EPA has quantified dermal exposure by workers. TSCA does not permit EPA to ignore exposures that it considers *de minimis*. EPA states that "there is low to medium confidence in consumer dermal exposure modeling due to uncertainties related to absorption and assumptions regarding impeded evaporation for particular COU." We agree and believe that EPA should revise this modeling to reflect more realistic consumer use scenarios.	
103	**PUBLIC COMMENTS:** EPA should consider providing additional discussion of the uncertainty in the occupational dermal exposure scenarios, and potentially calculating the range of possible exposures utilizing different models.	
Uncertainties in dermal modeling were not adequately addressed		
99	**PUBLIC COMMENTS:** EPA admits that its absorption rate modeling was uncertain because "there is a large standard deviation experimental measurement, which is indicative of the difficulty in spreading a small, rapidly evaporating dose of TCE evenly over the skin surface."	As with all modeling assessments, there is some level of uncertainty. Uncertainties in regards to dermal modeling are discussed in both the Risk Evaluation and the Supplemental File: Environmental Releases and Occupational Exposure. The EPA appreciates the submission of this comment. The EPA will consider additional alternative model selections, modeling assumptions and empirical dermal exposure studies in future assessments.
94	**PUBLIC COMMENTS:** The TCE risk evaluation would be strengthened by refinements to the methodology of the exposure characterization. When utilizing WOE approaches to develop appropriate input parameters, models may be more reliable than low-quality monitoring data. • Alternative model selections and more well-informed inputs indicate that dermal exposures are likely substantially lower in the industry	

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	than was estimated by EPA. • EPA should consider the incorporation of additional exposure modeling in the revised risk evaluation that reflects well characterized industrial handling practices. • At a minimum, the risk evaluation should include discussion of the impacts of these assumptions on the level of confidence in the overall estimates, and the degree to which the assumptions are more than adequately protective. • Given the many uncertainties inherent in the TCE dermal assessment, EPA should also investigate whether an empirical study of dermal exposure to TCE can be conducted, and the findings incorporated into the revised draft.	
ONUs: EPA's assumptions of ONU exposure scenarios and levels of exposure require justification		
SACC	**SACC COMMENTS:** Recommendation: Clarify the distinction between workers and ONUs for all COCs. In Table 2-23, it is not clear why chemists are considered ONUs (even analytical chemists?), as are engineering technicians, or shoe and leather workers. In small commercial operations, the same person can be both a retail worker (ONU) and worker-operator.	EPA has not found additional reasonably available information or data to explore different categories of ONUs beyond the ONU categories presented in this Risk Evaluation. In Uncertainties section 4.3.2, EPA added the uncertainty "ONUs are likely a heterogeneous population of workers, and some could be exposed more than just occasionally to high concentrations." Also, workers at small facilities are not excluded.
56, 108, 100	**PUBLIC COMMENTS:** The commenter supports EPA's decision to assume that ONUs will not wear respirators; however, EPA may still have underestimated exposure to ONUs. • EPA assumes central tendency exposures for ONUs in any case where it does not have monitoring data or modeling specific to	EPA has revised the Risk Evaluation to discuss uncertainties associated with assumptions related to ONUs. EPA acknowledges that workers and ONUs may not stay within their respective work zones for the entire workday, and that exposures

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	ONUs and provides no estimate of high-end risk for ONUs. These cases are those where the "population" column in Table 4-54 identifies the population as "ONU (upper limit)." EPA then determines ONUs face an unreasonable risk only if its central tendency risk estimate for workers (carried over to ONUs) exceeds its benchmark. • Where EPA does have data to estimate exposure of ONUs specifically, EPA assumes that they are only present in the "far field zone" – *i.e.,* outside of the "near field" workers' zone. However, ONUs may not stay within the "far field zone." • EPA assumes that ONUs will have no dermal exposures, an assumption that is unfounded for cleaning workers and skilled trade workers. • Particularly over a short period (*e.g.,* response to a spill or equipment maintenance), ONU exposures may be as great as or greater than those of other workers, and ONUs are even less likely to be provided PPE. EPA's failure to collect ONU-specific data and its reliance on central tendency exposure estimates thus understates the risks to ONUs.	for ONUs can vary substantially. Most data sources do not sufficiently describe the proximity of these employees to the exposure source. As such, exposure levels for the "ONU" category will have high variability depending on the specific work activity performed. It is possible that some employees categorized as "ONU" have exposures similar to those in the "worker" category depending on their specific work activity pattern. ONUs are likely a heterogeneous population of workers, and some could be exposed more than just occasionally to high concentrations. For the risk evaluation, ONUs were defined as not routinely handling the chemical that is handled by the workers. Therefore, dermal exposures for ONUs were excluded. While spills and leaks generally are not included within the scope of a TSCA risk evaluation, maintenance staff are considered a subset of ONUs and as such are not excluded from the risk evaluation.
56, 108	**PUBLIC COMMENTS:** • EPA has provided no empirical basis for its arbitrary assumption that ONUs will never be exposed at levels higher than the central tendency exposure workers experience. EPA's approach is at odds with its obligation under TSCA to conduct risk evaluations that ensure protection of PESS, which TSCA explicitly defines as including workers. • EPA represents its high-end estimates as "generally intended to cover individuals or sub-populations with greater exposure," while its	EPA has revised the Risk Evaluation to discuss uncertainties associated with assumptions related to ONUs. EPA acknowledges that workers and ONUs may not stay within their respective work zones for the entire workday, and that exposures for ONUs can vary substantially. Most data sources do not sufficiently describe the proximity of these employees to the exposure

	central tendency estimates apply to the "average or typical exposure" that people experience (p. 655). TSCA would not permit EPA to protect against only the "average or typical exposure;" in fact, when it comes to workers, ONUs, and other PESS, EPA is required to protect all of them.	source. As such, exposure levels for the "ONU" category will have high variability depending on the specific work activity performed. It is possible that some employees categorized as "ONU" have exposures similar to those in the "worker" category depending on their specific work activity pattern. ONUs are likely a heterogeneous population of workers, and some could be exposed more than just occasionally to high concentrations. See also Sections 2.3.3, 3.2.5.2, and 4.4.1 in the risk evaluation for further discussions of PESS. EPA disagrees that the potentially exposed or susceptible subpopulations identified for each chemical substance must include workers. TSCA section 3(12) lists examples of human receptors that may be considered PESS but provides for EPA to identify the relevant subpopulations for each chemical substance.
100, 108	**PUBLIC COMMENTS:** EPA acknowledges that it has virtually no data on ONU exposures, and the broad range of workers that EPA defines as ONUs is too large to support any single classification. For example, supervisors have very different exposure patterns than skilled trade workers and cleaning workers, and thus face very different risks from TCE. • Information on activities where ONUs may be present are insufficient to determine their exposures.	EPA has not found additional reasonably available information or data to explore different categories of ONUs beyond the ONU categories presented in this Risk Evaluation.
ONUs: EPA should collect additional ONU exposure data		
SACC	**SACC COMMENTS:** Recommendation: Explore the use of area monitoring samples and estimates of far field modeling concentrations for deriving ONU exposure estimates.	Where data was reasonably available, both area monitoring data and far-field modeling data were used to estimate ONU exposures.

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	Monitoring data reports frequently have area samples (also called static samples) collected away from the worker's location. These data could be explored as potential indicators of ONU's exposures.	
108	**PUBLIC COMMENTS:** During the SACC meeting, several reviewers raised concern over EPA's lack of sufficient occupational exposure data especially with regards to ONUs and suggested that EPA undertake a more concerted effort to acquire data from OSHA, NIOSH, and companies to fill these gaps. • One reviewer suggested that OSHA or NIOSH inspection data could be helpful in understanding where ONUs are located in facilities, helping to refine the near field versus far field assumptions. If these agencies do not have applicable data, EPA could request that they collect such data moving forward. • Another reviewer noted that the same data gap issues have arisen in multiple draft risk evaluations and will continue to arise unless addressed; he suggested that EPA begin looking forward to the next 20 chemicals slated for risk evaluations to proactively fill data gaps by better collaborating with NIOSH and OSHA.	EPA thanks the commenter for the suggested data sources. EPA consults regularly with its federal partners and will consult with OSHA and NIOSH on this topic for future risk evaluations.
Improved discussion/consideration of hierarchy of engineering controls		
SACC	**SACC COMMENTS:** Recommendation: Improve the discussion of the exposure control hierarchy. The draft risk evaluation's discussion of the exposure control hierarchy should be more complete, specifically noting the PPE is the third stage of protection after establishment of proper engineering and administrative controls. EPA should also present data demonstrating relatively poor adherence to guidelines and supporting recommendations for worker protection, not just provide a reference. At a minimum, the discussion should provide a table summarizing the type of gloves recommended for TCE by NIOSH, OSHA, and product manufacturers, both for handling neat TCE and TCE-containing mixtures.	Section 2.3.1.2.6 of the Risk Evaluation discusses the hierarchy of controls and that PPE is the last stage of protection.
80, 100	**PUBLIC COMMENTS:**	A hierarchy of controls is a method for

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	The hierarchy of controls has been endorsed by NIOSH, the American Society of Safety Engineers, the American Industrial Hygiene Association, ACGIH, the American Public Health Association, the American Federation of Labor and Congress of Industrial Organizations, and many others. OSHA has incorporated the hierarchy of controls into all of its health standards, and EPA has endorsed this risk management approach. It calls for the use of elimination, substitution, engineering controls, administrative controls, and lastly PPE. That order is predicated on well-established observations that PPE is the hardest control to effectively implement and has the highest failure rate. • While the draft risk evaluation pays lip service to the hierarchy of controls – stating that PPE should be the "last means of control," to be used only "when the other control measures cannot reduce workplace exposure to an acceptable level" – EPA's assumption of PPE use prior to the consideration of other risk management tools is fundamentally at odds with this approach. • Given the broad acceptance of this methodology when conducting occupational risk assessment, EPA's deviation from the hierarchy of controls violates EPA's obligation to use the best available science in TSCA risk evaluations.	eliminating workplace hazards. While EPA has assessed the extent to which certain exposure reduction tools that it assumes to be in place may be reducing risks to workers, application of the methodology of the hierarchy of controls is not relevant to risk evaluations. EPA will manage unreasonable risks presented by chemical substances when the Agency undertakes regulatory action for COUs determined to have unreasonable risk. Utilization of the hierarchy of controls to recommend or require risk management actions in the risk evaluation would be premature and inappropriate.
Consumers: Consumer COU/exposure scenarios/pathways require clarification or are not valid/complete		
SACC	**SACC COMMENTS:** Recommendations: (1) Include a more detailed description of the process used for identifying consumer COUs and TCE-containing products. (2) Review current uses of the 33 reported commercial, industrial, and consumer COUs and identify all of the TCE-containing products for each of the consumer use scenarios. • The Committee concluded that there is insufficient description about the process used for identifying consumer COUs and products containing TCE. One member of the Committee noted that the draft risk evaluation is clear in explaining differences between COU categories and products identified in the draft risk evaluation and those identified in the problem formulation (U.S. EPA, 2018).	The Risk Evaluation describes the sources used to identify COUs, including EPA's *Use and Market Profile for Trichloroethylene*, (EPA-HQ-OPPT-2016-0737-0056). The *Use and Market Profile for Trichloroethylene* provides a description of the process EPA used to identify COUs (including consumer COUs), including use the of EPA databases from Chemical Data Reporting, the Toxic Release Inventory, and the National Emissions Inventory. Section 3 of the report further details the process EPA used to

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	• The draft risk evaluation references the Use and Market Report and Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: TCE (U.S. EPA, 2017c), but the report does not describe how specific consumer products were identified. It is not clear when this report was updated. • The draft risk evaluation does not describe in enough detail and specificity how comprehensive and systematic the search was for this information. On p. 142, the draft risk evaluation states: "Additional online research was undertaken following problem formulation to confirm TCE concentrations and compile a comprehensive list of products that may be available to consumers for household use." What kind of "online research" was performed? • Similarly, on p. 179 the statement: "Additional sources of product information were evaluated, including the NIH Household Product Survey and EPA's Chemical and Products Database (CPDat), as well as available product labels and safety data sheets (SDSs)" does not provide enough details to know how comprehensive and systematic the search was. A Committee member noted that the National Institutes of Health (NIH) Household Product Survey is no longer maintained by the NIH, and wondered what steps are being taken going forward to ensure that products are identified in a systematic and comprehensive manner.	supplement information from these databases, including internet searches for consumer products. In addition, the Risk Evaluation notes that EPA made use of public meetings, and meetings with companies, industry groups, chemical users and other stakeholders to aid in identifying conditions of use and verifying conditions of use identified by the EPA. Statements in the Risk Evaluation implying "Additional online research" or "Additional sources" conducted after Problem Formulation have been rewritten to clarify that research subsequent to Problem Formulation was conducted to confirm information identified in prior searches. There are limited available product databases and they are not necessarily complete nor consistently updated and general internet searches cannot guarantee entirely comprehensive product identification. Therefore, it is possible that the entire universe of products may not have been identified, or that certain changes in the universe of products may not have been captured, due to market changes or research limitations. EPA has added language clarifying this in Section 3.2.7.2 of the Risk Evaluation.
SACC	**SACC COMMENTS:** • It is unclear if the IRTA (2007) report is a good proxy for TCE-based spot remover, as the product was prohibited by California Air Resources Board (CARB, 2019) for that use in 2012. Additional products may have also been reformulated in part due to California	The IRTA (2007) study was used to develop (for CalEPA and EPA Region IX) annual per-site use rate information for an occupational exposure scenario as described in section 2.14.3.3.2 of the

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	Proposition 65. • Another Committee member noted that a surrogate product is used for film cleaner and toner aid use scenarios, but a simple Google internet search reveals the commercial availability of TCE-containing film cleaners (*i.e.,* brands such as Edwal, Tetenal, etc.) both in liquid and spray forms, and toner aid (*e.g.,* brand Sprayway; SDS online; see example: http://www.spraywayinc.com/content/toner-aide).	Supplemental Information File Environmental Releases and Occupational Exposure Assessment (Inhalation Exposure Assessment Results Using Modeling – Spot Cleaning). All weight fractions used in this evaluation are derived from SDSs for actual TCE-containing products. The "surrogate product data" used from Westat represent the most current, nationally relevant data source available for a range of the evaluated conditions of use, namely for data on length of time a product was used, the room of use, and the mass of product used. These durations and amounts are intended to cover the spectrum of possible users ranging from low to high intensity users as described in the document.
SACC	**SACC COMMENTS:** Recommendation: Reexamine the pepper spray use scenario. • Committee members indicated that it is unclear whether any of the pepper spray products remain available in the consumer market. It is not clear what efforts were taken to ensure the scenario described on p. 148, footnote 12 in Table 2-28 is reflective of actual usage. EPA needs to verify and/or determine the concentration of the existing pepper spray products, and review if this and other product use patterns appear reasonable. • Another Committee member considered the assumption of only one gun in the gun scrubber use scenario not well justified and not sufficiently conservative.	EPA has updated the pepper spray scenario to include additional variance in user intensity scenarios based on different mass inputs (Table 2-29), resulting in addition of two additional scenarios reflective of a higher use amount. EPA acknowledges that variability exists in modeling assumptions of user scenarios for gun scrubber. As stated in Section 2.3.2.6.2, "this mass input may not appropriately capture consumers cleaning multiple guns in a day…." While the Westat product category does not align closely with this specific use, the duration data was deemed reasonable for modeling.
SACC	**SACC COMMENTS:**	

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	One Committee member suggested including TCE inhalant as a consumer exposure. However, other members indicated that intentional misuse of products is not considered a COU under TSCA.	EPA would not generally consider intentional misuses (*e.g.,* inhalant abuse), as a "known" or "reasonably foreseen" activity. Without this exclusion, the concept of "conditions of use" would likely result in no meaningful limitation on EPA risk evaluations, and risk evaluations could present unmanageable challenges—an outcome that EPA does not expect Congress intended.
56, 108	**PUBLIC COMMENTS:** EPA excludes "paints and coatings for consumer use" but continues to analyze these COUs in the industrial and commercial context. • EPA should analyze consumer uses in these circumstances. TCE's use in the industrial and commercial context makes it at least reasonably foreseen that TCE is, or could be, used in the same manner in the consumer context. Even where a product is "labeled for industrial use," it may be reasonably foreseeable that the product may ultimately be used by a consumer. During the SACC meeting, EPA explained that the exclusion was due to EPA's promulgation of a SNUR on certain consumer uses of TCE, implying that the SNUR *prohibits* consumer use of TCE in paints and coatings. This is untrue; the SNUR does not place any restrictions on such use; any actual restriction would require further Agency action subsequent to review. • The existence of a SNUR is insufficient to conclude that these uses will not occur or are not "reasonably foreseeable. • EPA has not adequately shown that these circumstances are not "reasonably foreseen" COUs. • Even if a ban on TCE's use in such consumer products were in place, absent specific steps to ensure that consumers cannot gain access to products intended for industrial or commercial uses, such use would still be "reasonably foreseen." • Non-occupational bystanders may be exposed to industrial or	EPA does not believe that paints and coatings for consumer use contain TCE. EPA did not identify any paint and coating products currently containing TCE through the searches of the internet, databases, and other sources used to identify uses and does not consider it an ongoing use. Furthermore, EPA developed a Significant New Use Rule (SNUR) on TCE in Certain Consumer Products (81 FR 20535) that was cited in the Problem Formulation for TCE. Persons subject to the SNUR are required to notify EPA at least 90 days before commencing any manufacturing or processing of TCE for a significant new use, including manufacture or processing of TCE for use in paints and coatings for consumer use. The required Significant New Use Notification (SNUN) provides EPA with the opportunity to evaluate the intended use. If EPA finds upon review of the Significant New Use Notice (SNUN) that the significant new use presents or may present an unreasonable risk (or if there is insufficient information to permit a reasoned evaluation of the health and

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	commercial uses of paints and coatings containing TCE during regular use, *e.g.,* during painting of residential spaces or houses or other buildings. • EPA cannot evade their duty by limiting its analysis to COU with evidence of current, ongoing use – such an interpretation limits EPA's analysis to "known" uses.	environmental effects of the significant new use), then EPA would take action under TSCA section 5(e) or (f) to the extent necessary to protect against unreasonable risk. EPA is only including use of TCE in industrial and commercial paints and coatings as a condition of use for TCE. Because U.S. EPA 2014 was developed prior to the SNUR and proposed rules for the ban of TCE in certain uses, it does not reflect ay market changes that may have occurred subsequent to its preparation. Finally, the Use and Market Report states that the list of products containing TCE within the report is not exhaustive and has not been updated. The Use and Market Report is meant to provide examples of products that contain TCE and their formulations where possible.
SACC	**SACC COMMENTS:** Recommendation: Clarify whether consumer paints and coatings no longer contain TCE. It is not clear if referenced U.S. EPA (2014) is reflective of likely market changes since the significant new use rule (SNUR) on consumer uses for TCE was implemented as well as the proposed rules for the ban of aerosol and vapor degreasing. Based upon a review of the 33 reported commercial, industrial, and consumer products listed in the Market and Use Report, 17 appear valid, 2 appear to no longer exist, and 13 are unclear as to current status. In addition, there are products that have not been captured in the draft risk evaluation. For example, the previously cited hoof polish product now is labeled as 'extremely flammable' and has likely been reformulated, and Berryman Products appears to have products formulated with TCE (www.berrymanproducts.com).	
108	**PUBLIC COMMENTS:** EPA excludes the oral route of exposure for consumers despite acknowledging potential for exposure via hand-to-mouth patterns.	As stated in the footnotes for Figure 1-5, mists of TCE will likely be rapidly absorbed in the respiratory tract or evaporate and not result in an oral exposure. Although less likely given the physical-chemical properties, oral exposure may also occur from incidental ingestion of residue on hand/body. Because oral exposure would be a very minor pathway relative to dermal and inhalation exposure.
108	**PUBLIC COMMENTS:**	

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	EPA excludes exposure to consumers from disposal. Congress consciously decided to specify that "disposal" is a COU under TSCA.	EPA evaluated and considered the impact of existing laws and regulations (*e.g.,* regulations on landfill disposal, design, and operations) in the problem formulation step to determine what, if any future analysis might be necessary as part of the risk evaluation. During problem formulation EPA analyzed the TRI data and examined the definitions of elements in the TRI data to determine the level of confidence that a release would result from certain types of disposal to land (*e.g.,* RCRA Subtitle C hazardous landfill and Class I underground Injection wells) and incineration. EPA also examined how TCE is treated at industrial facilities. EPA did not include emissions to ambient air from commercial and industrial stationary sources, which are under the jurisdiction of and addressed by Section 112 of the Clean Air Act. EPA did not include emissions to ambient air from municipal and industrial waste incineration and energy recovery units in the risk evaluation, as they are regulated under section 129 of the Clean Air Act. EPA did not include disposal to underground injection, RCRA Subtitle C hazardous waste landfills, RCRA Subtitle D municipal solid waste (MSW) landfills, and on-site releases to land from industrial non-hazardous waste and construction/demolition waste landfills in this Risk Evaluation. These methods of disposal fall under the jurisdiction of and are addressed by other EPA-administered statutes and associated regulatory programs.

47	**PUBLIC COMMENTS:** One consumer COU was excluded from the final list (lace wig and hair extension glues) because, after consultation with the FDA, it was determined that it falls outside the scope of EPA's jurisdiction. • This does not mean that exposure attendant to that use should be excluded from the exposure assessments for consumers in the relevant subpopulation.	Under TSCA § 3(2)(B)(vi), the definition of "chemical substance" does not include "any food, food additive drug, cosmetic, or device (as such terms are defined in section 201 of the Federal Food, Drug, and Cosmetic Act) when manufactured, processed, or distributed in commerce for use as a food, food additive, drug, cosmetic, or device." EPA has concluded that lace wig and hair glue is used as a cosmetic, and has concluded that this use falls within the aforementioned definitional exclusion and is not a "chemical substance" under TSCA.
47	**PUBLIC COMMENTS:** The current assessment included three consumer uses that had been excluded from the 2014 TCE Risk Assessment list. • This is seen to be a wise choice because these three COUs were determined to pose an unreasonable risk to consumers and also to bystanders, and, therefore, are targets for risk management, most appropriately a ban on all those uses.	EPA acknowledges this comment.
99	**PUBLIC COMMENTS:** EPA concedes that its risk estimates for consumers may be understated because they do not take into account the continuous presence of TCE in outdoor and indoor air.	EPA acknowledges this comment and agrees there may be an underestimation of risk. Additional discussion of this underestimation is found in Sections 2.3.2.6.1 and 4.4.2.
Consumers: Additional consumer data considerations		
SACC	**SACC COMMENTS:** Recommendation: Consider exploring the wealth of information available in the internet on do-it-yourself (DIY), hobbies, and home-based production of items for sale to get more data on products used by consumers who are likely high-frequency users. Although the Committee could not identify additional sources of data for specific COU and was not aware of any specific databases, it is likely	As noted in the document entitled EPA's Responses to Public Comments Received on the Scope Documents for the First Ten Chemicals for Risk Evaluation under TSCA (EPA-HQ-OPPT-2016-0723-0067), EPA conducted extensive and varied data gathering activities for

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	that these data exist. Some of the large general population exposure assessment studies cited in the draft risk evaluation also administered questionnaires about residential activity patterns and the use of some types of products. This literature could be explored to obtain information on product type use, though not specific products.	each of the first 10 chemicals, including: • Extensive and transparent searches of public databases and sources of scientific literature, government and industry sector or other reports; • Searches of EPA TSCA 8(e), Chemical Data Reporting, and other EPA information holdings; and CBI submission holdings; • Searches for Safety Data Sheets (SDSs) using the internet, EPA Chemical and Product Categories (CPCat) data, the National Institute for Health's (NIH) Household Product Database, and other resources in which SDS could be found; • Preparation of a market analysis using proprietary databases and repositories; • Outreach meetings with chemical manufacturers, processors, chemical users, non-governmental organizations, trade organizations, and other experts, including other State and Federal Agencies (*e.g.,* Dept of Defense, NASA, OSHA, NIOSH, FDA and CPSC); and EPA published conditions of use documents, scope documents, and problem formulation documents to solicit information generally from industry, nongovernmental organizations, and the public.
SACC	**SACC COMMENTS:**	EPA has conducted public outreach and

	Recommendation: Scrutinize the products included in the ATSDR (2019) Toxicological Profile for TCE content or reformulation. • A member of the Committee indicated that the ATSDR (2019) Toxicological Profile for TCE included typewriter correction fluid, drain cleaners, spray paint, and paint strippers as uses. These should be considered. It is not clear in the draft risk evaluation whether all products included in the Toxicological Profile underwent careful scrutiny (revalidation) by EPA.	literature searches to collect information about trichloroethylene's conditions of use and has reviewed reasonably available information obtained or possessed by EPA concerning activities associated with trichloroethylene, including information on uses in the ATSDR Toxicological Profile. The conditions of use included in the risk evaluation include uses for which manufacturing, processing, or distribution in commerce is intended, known to be occurring, or reasonably foreseen to occur.
SACC, 108	**SACC COMMENTS:** Recommendation: Consider updating the Westat survey data (U.S. EPA, 1987) to verify that use patterns and building-related parameters reflect current consumer use patterns and housing construction. The committee was unanimous that at least some consumer use patterns are likely to have changed since the survey data was collected. The size of homes has also changed with a trend to larger homes and more open floor designs, as to increasingly tighter structures that may affect air exchange rates.	Conducting a national survey of consumer uses and behaviors was infeasible to support the TCE risk evaluations. Absent a time-consuming update, the data used from Westat still represent the most current, nationally relevant data source available for a range of the evaluated conditions of use. EPA notes there are limitations and uncertainties associated with this Westat dataset.
Consumers: EPA should consider chronic scenarios for consumer exposure		
SACC, 99, 108	**SACC COMMENTS:** Recommendation: Characterize TCE chronic risk to consumers and add a discussion of chronic non-cancer risks. The committee disagrees with EPA's basis for their decision not to characterize chronic risks. Several Committee members suggested that some consumers are likely to be exposed more frequently and more pervasively to emissions from these products than indicated by the Westat survey data (U.S. EPA, 1987). • Certain high-exposed consumers (hobbyists, home businesses, etc.) are likely to use more than one TCE-containing product on the same	Scenarios for conditions of use associated with products containing TCE include a wide range of usage intensities with ranges in weight fractions, time of use, and mass of product used. While the actual use of the product only occurs a single time during the evaluation period a given consumer user can encounter inhalation exposures during both the use period and also following use through the prescribed movement

	day and/or multiple and consecutive days. • The Westat survey was unlikely to capture the true distribution of use frequency for high-end users (oversampling would be been required to obtain a reliable estimate of use patterns). • It is likely that contributions to indoor air concentrations (and, therefore, exposures) persist for longer periods of time than assumed by EPA from sources such as carpet spot cleaners and fabric sprays. Products stored in homes after use may emit low levels of chemical into the indoor atmosphere resulting in additional chronic exposure. **SACC COMMENTS:** Recommendation: The uncertainty in consumer risks from high-end periodic exposures combined with background air and water concentrations should be better characterized and if possible, sensitivity to assumptions and data uncertainties addressed. On p. 322, the draft risk evaluation indicates that risks cannot be ruled out for consumers exposed from high-end frequency of product use that is periodic. Associated risks could not be estimated due to the uncertainty in the extrapolation from continuous exposure studies in animals. The Committee expressed concern that periodic exposures combined with background exposures may leave consumers with higher risks than calculated in this draft risk evaluation. **PUBLIC COMMENTS:** • Other chronic users may be artists who work at home, home renovators, and consumers who maintain and repair vehicles. EPA could determine overall exposure levels from recurring consumer use of multiple TCE-containing consumer products and then estimate risks of cancer, developmental/reproductive toxicity, kidney effects, and immunotoxicity to consumers.	about the house. EPA assumes that exposure is not chronic in nature, the assumption is discussed in Section 2.3.2.2 of the Risk Evaluation. Chronic exposure scenarios resulting from long-term use of household consumer products were not evaluated as these events are likely to be relatively infrequent with short durations of use. This assumption is supported by product use frequencies reported within the Westat survey (1987) for evaluated conditions of use that give central tendency frequencies that were considered to be too low to create chronic risk concerns. In addition, the short half-life of the chemicals in the body does not result in significant accumulation between uses on different days. EPA directly identifies the uncertainties, such as the fact that exposure estimates may underestimate exposure to individuals who are involved with do-it-yourself projects as well as recognition that consumer practices are moving toward more do-it-yourself work. TSCA Section 6(b)(4)(F)(iv) instructs EPA to factor into TSCA risk evaluations "the likely duration, intensity, frequency, and number of exposures under the conditions of use." This suggests that activities for which duration, intensity, frequency, and number of exposures cannot be accurately predicted or calculated based on reasonably available information were not intended to be the focus of TSCA Risk Evaluation. Since reasonably available
56, 108	**PUBLIC COMMENTS:** EPA assumes a single dermal exposure event per day for consumers. • This assumption is particularly problematic for "do-it-yourselfers,"	

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	which EPA acknowledged may be exposed more than once per day. EPA fails to actually address this scenario in calculating exposure and risk estimates.	information was not identified to inform these and other parameters, and as recognized by SACC the absence of data leaves it uncertain how to develop a worst-case scenario, storage of consumer products was not evaluated in this Risk Evaluation.
56, 108, 99	**PUBLIC COMMENTS:** EPA fails to assess any chronic exposures to consumers despite acknowledging in the draft risk evaluation they are expected to occur. • EPA thus fails to address consumer risk for cancer, developmental toxicity, kidney effects, and immunotoxicity. • While chronic exposure may not be typical for consumers, EPA's failure to assess DIY users as a "potentially exposed or susceptible subpopulation" is troubling, particularly because it considered DIY users as a sentinel exposure. EPA's assumptions about consumer exposure are likely to significantly underestimate the risks they face. EPA needs to conduct a sensitivity analysis regarding these assumptions in the context of this risk evaluation, which is different than the sensitivity analysis EPA indicates was done on the model itself.	
49, 99	**PUBLIC COMMENTS:** EPA's risk evaluation assumes that consumers only have acute exposure to TCE. However, the evidence of ongoing TCE concentrations in indoor air indicates that chronic exposure is also occurring and therefore consumers are at risk for cancer and other chronic health effects that EPA fails to address. • Since exposure to TCE in ambient air and contaminated drinking water is continuous, if EPA included these pathways, it could not limit its evaluation to acute risks to consumers, it would need to address long-term exposure scenarios.	
Consumers: Comments on Consumer Exposure Model (CEM) parameters/estimates; additional suggestions		
SACC	**SACC COMMENTS:** Recommendation: Consider developing CEM exposure estimates for bystanders present in Zone 1 for scenarios where it is likely that the bystander could be in the same room as the user.	EPA acknowledges that consumer bystanders were not assumed to be exposed in same room as the users. Additional language has been added to the uncertainty discussion in Section 2.3.2.6.

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	In the CEM model members of the Committee were concerned about the assumption that bystanders remain in Zone 2 while the product is in use, without providing adequate justification for this assumption, which could result in underestimation of bystander exposures. • One Committee member suggested that bystanders should be treated similarly to how ONUs are treated in the OESs, and was unclear why "near-field" and "far-field" zone assumptions could not be applied to consumer users and bystanders in the same room (in addition to the alternative of assuming the zones correspond to two separate rooms).	EPA will consider this refinement to the consumer modeling approach for future evaluations.
SACC	**SACC COMMENTS:** Recommendation: Perform a sensitivity analysis on inputs to the consumer exposure model to address uncertainties in representativeness of model outputs. EPA's conclusion that "Certain inputs to which the (consumer exposure) model outputs are sensitive, such as zone volumes and airflow rates, were not varied across product-use scenarios. As a result, model outcomes for extreme circumstances such as a relatively large chemical mass in a relatively low-volume environment likely are not represented among the model outcomes. Such extreme outcomes are believed to lie near the upper end (*e.g.,* at or above the 90th percentile) of the exposure distribution," represents a source of uncertainty, and the limited discussion provided to be inadequate.	The overall CEM model had a sensitivity analysis conducted for evaluation of which scenario specific inputs influenced inhalation and dermal exposure results. Within this section, EPA describe that the full description of this sensitivity analysis is available in Appendix C of the CEM User's Guide (U.S. EPA, 2019a). As described in Appendix C, elasticity was evaluated by altering model input parameters by a 10% increase. Due to the number of parameters evaluated, the calculated elasticities are not included in the risk evaluation but are available for review in Tables D2-D8 and Figures D1-D15 in Appendix C of the User's Guide available here: https://www.epa.gov/sites/production/files/2017-06/documents/cem_user_guide_appendices.pdf .
Appropriateness of exposure uncertainty discussion		
SACC	**SACC COMMENTS:** Recommendation: Discuss all of the biases and uncertainties inherent in OSHA and non-OSHA, and foreign monitoring data for exposure estimation. • In particular, German data were used as a surrogate for unloading	EPA identifies the uncertainty of representativeness as a primary uncertainty for each occupational exposure scenario that includes monitoring data. The Uncertainties

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	and repacking, and degreasing. There is potential for exposures in Germany to be lower because of tighter controls in response to the stricter occupational exposure regulations. This issue and corresponding limitation of using the German data should be specifically discussed.	section 4.3.2.1 provides detailed discussion of this potential bias and notes that limited data sets may potentially underestimate or overestimate exposures. Foreign data is scored following the data quality ratings in EPA's *Application of Systematic Review in TSCA Risk Evaluations*.
103	**PUBLIC COMMENTS:** EPA should provide additional discussion of the uncertainty in the occupational dermal scenarios.	Uncertainty in dermal exposure estimates is included in Sections 2.3.2.7 and 4.3.2.3 of the Risk Evaluation.
80	**PUBLIC COMMENTS:** EPA should develop uncertainty estimation methods to define potential distributions of PPE usage and performance. These distributions should then be included as parameters in the Monte Carlo occupational exposure assessment modeling. Several studies have proposed methods for characterizing uncertainty in respirator performance and usage.	EPA appreciates the comment and may consider potential distributions of PPE usage and performance as data availability allows.
Appropriateness of exposure confidence ratings		
SACC	**SACC COMMENTS:** Recommendation: Provide more detail on the confidence ratings used in the tables for inhalation and dermal exposures. • Committee members liked the framework of variability and uncertainty for presenting strengths and limitations in risk characterization estimates for consumers. However, it is unclear how the final confidence levels are derived. Footnotes in Tables 2-71 and 2-72 do not provide enough detail to clarify the process that leads to a high, moderate or low confidence for each specific component of the risk characterization and consumer use in these tables. • One Committee member noted that statements such as: "The exposure durations modeled could exceed the duration of such dermal contact, therefore, the higher-end durations may result in an overestimation of dermal exposure" should acknowledge the possibility of underestimation unless a specific reason is provided for why the potential error is one-sided.	Tables 2-85 and 2-86 lay out the factors that contributed to the overall confidence rating for each exposure scenario evaluated, such as model application, default values, and user-selected inputs (*e.g.,* mass, duration, weight fraction, and room of use). Consideration of the confidence in each of these displayed factors underlies the overall confidence score in a scenario. Section 2.3.2.7 discuss sources of uncertainty and assumptions that may lead to overestimation and underestimation of exposure.

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56, 108	**PUBLIC COMMENTS:** The errors in EPA's characterization of exposure monitoring systematic review ratings call into question EPA's ultimate "overall confidence" ratings for the inhalation exposure estimates presented in Table 2-26	EPA is in the process of seeking peer review of its Systematic Review protocol, and the confidence rating system may be addressed in future updates.
Exposure – other		
56, 108	**PUBLIC COMMENTS:** EPA did not establish that the exposures it analyzed represent the "plausible upper bound of exposure relative to all other exposures" within the relevant categories.	The purpose of risk evaluation under TSCA is "to determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other nonrisk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator, under the conditions of use." TSCA section 6(b)(4)(A). EPA described background exposure in the uncertainties section acknowledging that the risk estimations in the Risk Evaluation may be underestimations, because background exposures and risk are not incorporated into the risk estimations for each COU.
47	**PUBLIC COMMENTS:** TCE exposure assessments and risk determinations should take into account cumulative exposures to perchloroethylene (and to the other chlorinated compounds listed in Table 3.4) where metabolites, endpoints, COUs, and ambient exposures co-exist. TCE's and perchloroethylene's COUs have significant potential for overlap; their COU categories are virtually identical as are many of the subcategories.	TSCA section 6(b)(4)(F)(ii) directs EPA to "describe whether aggregate or sentinel exposures to a chemical substance under the conditions of use were considered, and the basis for that consideration" in risk evaluations. EPA defines aggregate exposures as the combined exposures to an individual from a single chemical substance across multiple routes (*i.e.,* dermal, inhalation, or oral) and across multiple pathways (*i.e.,* exposure from different sources).

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		40 CFR 702.33. EPA defines sentinel exposures as the exposure from a single chemical substance that represents the plausible upper bound of exposure relative to all other exposures within a broad category of similar or related exposures. 40 CFR 702.33. EPA considered the reasonably available information and used the best available science to determine whether to consider aggregate or sentinel exposures for a particular chemical. EPA has determined that using the high-end risk estimate for inhalation and dermal risks separately as the basis for the unreasonable risk determination is a best available science approach. There is low confidence in the result of aggregating the dermal and inhalation risks for this chemical if EPA uses an additive approach, due to the uncertainty in the data. EPA does not have data that could be reliably modeled into the aggregate, which would be a more accurate approach than adding, such as through a PBPK model. Using an additive approach to aggregate risk in this case would result in an overestimate of risk. Given all the limitations that exist with the data, EPA's approach is the best available approach.
56	**PUBLIC COMMENTS:** EPA dismisses unreasonable risk based on bias assessment of exposure estimates by choosing only to emphasize the potential for data sources to overestimate exposure, while ignoring the potential for similar factors to underestimate exposures.	EPA considered the weight of scientific evidence and presented its assessment of direction of uncertainty for exposure estimates in Sections 2.3.1.3 and 2.3.2.6.

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5. Human Health Hazard

Human Health Hazard
Charge Question 5.1: EPA performed a weight of evidence assessment for the endpoint of developmental cardiac defects based on available epidemiological, in vivo animal, and mechanistic data. EPA concluded that the available literature supported positive overall evidence that TCE may produce cardiac effects in humans (Section 3.2.4.1.6 and Appendix G.2); however cardiac defects after developmental exposure were not observed consistently across the available in vivo animal studies. The Charles River dissection methodology differed from Johnson et. al. (2003), resulting in reduced sensitivity to the full range of cardiac defects compared to Johnson et al. (2003) and other studies. Therefore, EPA concluded that the Charles River study did not adequately recapitulate the methodology of the Johnson et al. (2003) study. Please comment on EPA's Weight of Evidence (WOE) analysis approach and conclusions for this endpoint, including EPA's analysis of the Charles River (2019) and Dawson (1993)/Johnson (2003) studies. **Charge Question 5.2:** Please comment on the assumptions, strengths and weaknesses of the dose-response approaches used to estimate the non-cancer risks to workers, occupational non-users, and consumers. Please also comment on whether EPA sufficiently justified its selections of BMRs for BMD modeling results and uncertainty factor values in deriving the PODs and benchmark margin of exposures (MOEs) (Sections 3.2.5.3.2 and 3.2.5.3.3). As part of this discussion, please comment on EPA's justification for selecting a 1% BMR for the cardiac malformation endpoint based on the severity of the endpoint (*i.e.,* potential mortality). **Charge Question 5.3:** EPA determined that the immune effects from Selgrade and Gilmour (2010) represent the best representative dataset to use for evaluating acute effects and the autoimmunity effects from Keil et al (2009) represent the best data set to use for evaluating chronic non-cancer effects (Section 3.2.6.4). a. Please comment on EPA's selection of these studies as the best representative endpoints, including consideration of the POD derivation and benchmark MOEs. b. EPA did not input the data on response to pulmonary infection from Selgrade and Gilmour (2010) into the TCE PBPK model due to uncertainty over the proper dose metric to be used. Therefore, EPA relied on standard methods for cross-species scaling (*i.e.,* blood:air partition coefficient for HEC, allometric scaling for HED) and accordingly reduced the default 10X UFA uncertainty factor to 3 (see Section 3.2.5.3.2). Please comment on whether this approach is appropriate and whether the UF is sufficient. c. EPA acknowledges that in using the Keil et al (2009) study, EPA is relying upon an early clinical marker to account for susceptibilities, and the endpoint is a precursor to adverse effects for autoimmunity. This LOAEL was considered in this context and the LOAEL to NOAEL uncertainty factor was reduced from 10 to 3X. In light of this, please comment on EPA's use of a 3x Uncertainty Factor for human variability and LOAEL to NOAEL extrapolation. **Charge Question 5.4:** EPA performed a meta-analysis on the published database for liver cancer, kidney cancer, and non-Hodgkins lymphoma (NHL), concluding that there was a statistically significant association between TCE exposure and all three cancers when

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accounting for various sensitivity analyses. Please comment on EPA's methodology and conclusions (Sections 3.2.4.2.1 and Appendix H).

Charge Question 5.5: For the cancer dose-response assessment, EPA derived an inhalation unit risk (IUR) and oral cancer slope factor (OSF) based on epidemiological kidney cancer data from Charbotel et al, 2006, adjusted upward to also account for the relative contribution of NHL and liver cancer. Per EPA Guidelines for Carcinogen Risk Assessment, overall, the totality of the available data/information and the WOE analysis for the cancer endpoint was sufficient to support a linear non-threshold model (Section 3.2.4.2.2). Please comment whether the cancer hazard assessment has adequately described the methodology and justification for the cancer dose-response approach, including the use of a linear model and the adjustments made for the other tumor sites (Section 3.2.5.3.4).

Charge Question 5.6: Please comment on EPA's application of the PBPK model to the dose-response analysis for all endpoints. Was the selection of dose metrics and percentile output selection appropriate when considering the sensitivity, uncertainty, and variability of the data (Sections 3.2.2 and 3.2.5)?

Charge Question 5.7: Have the most scientifically robust critical health effects and corresponding PODs been identified for TCE? Are there additional data regarding other health effects for TCE that EPA needs to consider? If data gaps exist in the TCE database, how could the uncertainty about sensitive health effects and critical windows of exposure be better accounted for in the risk characterization (Sections 3.2 and 4.3.2)?

Charge Question 5.8: Please comment on any other aspects of the human health hazard assessment that have not been discussed, including the data quality evaluation and the characterization of all assumptions and uncertainties (Section 3.2).

#	Summary of Comments for Specific Issues Related to Charge Question 5	EPA/OPPT Response
Johnson et al. (2003)		
SACC	**SACC COMMENTS:** Committee members had differences in opinion concerning the adequacy of the Dawson/Johnson studies. These studies have several significant problems in their design and execution despite being scored as medium quality. For example, Johnson et al. (2003) used pooled data for controls from multiple experiments conducted over 6 years. Some members felt this study lacked credibility and should not be relied on by EPA. Several Committee members commented that Johnson et al. (2003) reported adverse cardiac effects at TCE exposure levels that were orders of magnitude lower than no-effect levels of other investigators. Other Committee members said it seems premature to completely dismiss Johnson et al. (2003), given that there are cardiac malformations (1-2 per	In considering the conflicting evidence and varied opinions concerning the validity and relevance of the cardiac heart defects (CHD) database, EPA has added text throughout the RE (Appendix F.1, Section 3.2.4.1.6, Section 3.2.5.3.1, Section 3.2.5.1.6, and Section 3.2.6.1) acknowledging the uncertainties associated with this endpoint. EPA acknowledges that while there is qualitative support for the endpoint, based on uncertainties in the dose-response for this endpoint and other considerations EPA has

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	1,000) in humans that are of unknown etiology. Another Committee member opined that EPA came to an appropriate conclusion after assessing the strengths and weaknesses of the Dawson/Johnson studies. Another member felt that it might not be possible to reach consensus. The Committee recognized that no systematic review can definitively answer the question of whether the issues with this study are severe enough to disallow its use in setting a non-cancer POD. Reasonable scientists have differed on this, and two reviews came to opposite conclusions. Wikoff et al. (2018) reviewed Johnson et al. (2003) and determined it was "not sufficiently reliable for the development of toxicity reference values." Makris et al. (2016) reviewed all the evidence for developmental cardiac effects and determined that Johnson et al. (2003) is "suitable for hazard characterization and reference value derivation."	selected immune endpoints as the best overall endpoints for risk conclusions (Sections 3.2.5.4.1, 3.2.6.1.1). However, various biological factors may lead to increased susceptibility to CHDs, (*e.g.,* maternal age). Therefore, CHDs are now classified as a PESS consideration and the associated POD and risk estimates are included in the RE in consideration of PESS groups. However, based on uncertainties in the dose-response for this endpoint and other considerations, EPA has selected immune endpoints as the best overall endpoints for risk conclusions (Sections 3.2.5.4.1, 3.2.6.1.1).
108, 99	**PUBLIC COMMENTS:** The Johnson et al. (2003) study is valid and appropriate for the derivation of toxicity values and risk estimates. This study has been repeatedly vetted, reviewed, and discussed by EPA and peer reviewers in previous assessments, including its limitations; in each case, the study was found to be sufficient for hazard identification and dose-response analysis. Its results are also wholly consistent with the findings of many other studies – including human, *in vitro* and *in vivo* studies – that also indicate congenital heart defects resulting from TCE exposure (see Makris et al., 2016; Runyan et al., 2019).	
105	**PUBLIC COMMENTS:** The Johnson et al. (2003) study provides relevant and positive evidence of that TCE can induce fetal heart defects and should not be discounted. • While there may be issues with the dose-response in the fetal heart defect study (Johnson et al., 2003), the WOE for fetal heart defects makes this an important developmental endpoint that should be considered in the quantitative assessment of the health hazards of TCE. • There is evidence from studies besides Johnson et al. (2003) that	

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	TCE-induced developmental cardiac toxicity effects may follow a non-monotonic dose response relationship, in which lower doses can produce greater effects than higher doses. In a recent mechanistic study on TCE-induced changes in gene transcription in the developing heart, a non-monotonic dose response was observed, and this is consistent with findings in other studies (Chen et al., 2020 and references within).	
99	**PUBLIC COMMENTS:** EPA classifies Johnson et al. (2003) as "medium quality" and suitable for use in risk determinations. The authors have responded in detail to the industry concerns, and reliance on the study is based on a careful review of this additional information. The study is essential for dose-response assessment without which calculation of MOEs for this endpoint would be impossible.	
80	**PUBLIC COMMENTS:** Cal/OSHA notes that while the SACC, in its discussion of fetal cardiac malformations on March 26, found both the Johnson et al. (2003) and Charles River Laboratory (CRL) studies problematic for dose response modeling, most committee members indicated that the Johnson et al. (2003) study was adequate for hazard assessment.	
99	**PUBLIC COMMENTS:** The 2016 EPA updated WOE assessment (Makris et al., 2016) reviewed available scientific literature on TCE developmental cardiac defects, reporting on the quality, strengths, and limitations of the available studies. This review concluded that the Johnson studies, augmented by detailed additional information about study design and conduct, were sufficient for dose-response analysis and determinations of risk. The study was considered suitable for use in deriving a POD. • The study has an appropriate design, was conducted by a relevant route of exposure (drinking water), covered the entire period of gestation covering the developmental window for the initiation of cardiac defects, and tested multiple exposure levels. • It had a robust, statistically significant dose-response relationship.	

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	Also, the highest dose lies at the lower end of doses that elicited substantial responses in other studies. Thus, "a hypothesis that the Johnson data represent a false positive or an anomalous dose-response pattern seems implausible, based on trend tests and comparison with studies that used higher doses." Makris et al. (2016) also addressed many of the concerns brought against the Johnson et al. (2003) study. • Based on a detailed methodological comparison of Johnson/Dawson and negative animal studies, differences in study methods (*e.g.,* route of exposure, vehicle, animal source or strain, or other factors) may have contributed to differences in the detection of cardiac malformations [between studies]. • Concerns about variability among litters were resolved in the method for data analysis: "The possibility of increased variability among litters due to temporal drift and perhaps other factors across time (overdispersion), was dealt with by using a standard method for clustered data. The dose-response trend was found to be highly significant after adjusting for overdispersion. Because the maximal observed response was 10%, models with plateaus of less than 100% were investigated and were found to not substantially change the general conclusions and results. Confidence in the dose-response relationship is supported by the increasing trend in response and by metabolite studies that demonstrate findings at higher dose levels."	
108	**PUBLIC COMMENTS:** Criticisms of the Johnson et al. (2003) study were discussed in the SACC meeting. Although some issues were identified, most members indicated that the Johnson et al. (2003) study was adequate for hazard assessment. • One SACC member noted that the combination of experimental data across several years (*i.e.,* pooling) is common, and well-accepted in epidemiological studies. Another SACC member indicated that observing the same effects several years apart is similar to replication and should be viewed as a strength. • One SACC member stated that the use of tap water as the negative	

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	control in one period of the experiment but the use of distilled water in another does not matter unless it can be demonstrated that one of these two types of water is directly causing the cardiac effects, which is highly unlikely. Another member highlighted that there is no plausible mechanism by which water would be responsible for cardiac defects.	
76, 79, 103, 72	**PUBLIC COMMENTS:** The Johnson et al. (2003) study has serious deficiencies that could not be corrected by the two published errata (Johnson, 2005, 2014) and one explanatory letter to the editor (Johnson et al., 2004). These diminish the reliability of the study for the purposes of risk assessment. • Potential maternal toxicity was not evaluated. Maternal clinical signs, body weights during gestation, and feed consumption were not reported; therefore, it is not possible to assess whether any of the fetal findings were secondary to maternal toxicity. • Potential developmental delay in the fetuses was not evaluated. Fetal weights were not reported, and it cannot be assessed whether any of the reported effects were due to the fetuses being at different stages of maturation than those in the control group. • "Litter effects" were not evaluated. Data were not recorded in a manner that allowed the laboratory to keep track of littermates. Data were not evaluated using the litter as the statistical unit. • Data regarding potential loss of TCE was not reported. Due to its high volatility, TCE likely was lost during the formulation of drinking water solutions, the transfer of formulations to water bottles, and during residence of the formulations on cages. In the CRL (2019) study, substantial TCE loss was observed and mitigated during formulation of water and transfer to bottles, indicating that this is a significant confounding factor. • In-life study was conducted over a 6-year period. The TCE treated groups and controls were not run concurrently, and the higher TCE dose groups were run 6 years prior to the lower TCE dose groups. Data for the higher TCE dose groups were first reported in Dawson	Follow-up personal communications from the study author (Johnson, 2008) provided maternal body weight data that show no significant difference among treatment groups in body weight gain that would suggest overt maternal toxicity. Simple developmental delay would not be expected to lead to observations of specific cardiac defects. Hearts were assessed at the time of birth and incomplete development at the time of birth would itself be a major endpoint. EPA acknowledges this issue as an important limitation of the Johnson lab studies in Appendix F.2.1 and Table_Apx F-1. (Johnson et al., 2003) provided data on average TCE loss across 24 hours, which was comparable or slightly less than the loss reported in (Charles River Laboratories, 2019). Substantial TCE loss would indicate that toxicity of TCE may have actually been underestimated, since any observed effects actually occurred at lower doses than nominally reported.

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	et al. (1993) in conjunction with data for 238 control fetuses (232 control hearts). None of the combinations of controls reported in the Johnson et al. (2005) erratum, however, equate to this initial number of controls, bringing into question the overall record-keeping related to this study. The study did not have a positive retinoic acid control. • Reported doses were not verified. It is not clear how doses were determined. Water consumption was reported to have been monitored by treatment group and maternal body weights were not measured. Body weights in pregnant rats are dynamic, and therefore, dose estimations could be highly inaccurate. • It was not verified that TCE was absorbed into maternal blood. • Cardiac dissection used a novel methodology and evaluation of fetal hearts was performed using a non-standard procedure.	The long duration of the study period is also acknowledged in Appendix F.2.1 and Table_Apx F-1. Some control experiments were run at the same time with treated groups, however both the authors and the Risk Evaluation acknowledge that data was pooled and compared from independent experiments. The number of controls at the time of (Dawson et al., 1993) publication may have included a partial group, however this is in fact an uncertainty that adds to the data reporting concerns, which are acknowledged in the Risk Evaluation. EPA agrees that doses were not analytically verified and this is an uncertainty that affects the precision of the dose-response analysis. This uncertainty applies to many studies however and does not exclude the positive results from consideration. Use of a novel dissection methodology that may have been more sensitive than traditional techniques is not a negative consideration.
94	**PUBLIC COMMENTS:** The extent to which EPA appears to support Johnson et al. (2003) at the expense of a balanced scientific review is not only inconsistent with the requirements of the Lautenberg Act but violates the fundamental principles of science. • The Johnson et al. data has not been replicated by any other laboratory. California Office of Environmental Health Hazard Assessment (OEHHA) also rejected the study as deficient for regulatory consideration.	EPA acknowledges that the original study publication would have scored lower than a medium in data quality, however EPA considered the reasonably available information for the set of studies in evaluating data quality. EPA determined that when accounting for subsequent errata and communications to EPA,

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	• The transparency problem and fact that an erratum had to be published should alone disqualify this as a study representing the "best available science." • Accepting the authors' claim in the 2014 erratum that exposure times cannot be confirmed for substantial amounts of either control or treatment data, it can be presumed that it is impossible to reconstruct a calculation of per litter incidence of cardiac malformations that is appropriately matched to concurrent controls, an analysis generally accepted as essential to interpreting outcomes of developmental toxicity study findings. The lack of data availability and clarity sufficient to construct key analyses associated with a study should disqualify the use of that study for regulatory purposes.	the overall strengths and limitations resulted in a study of medium quality.
94	**PUBLIC COMMENTS:** In Johnson et al. (2003), the abnormalities in rats dosed at 1100 ppm (10.4%) were statistically higher than at 1.5 ppm (5.5%), but those dosed at 1.5 ppm were not statistically different from the controls. Thus, no meaningful dose-response relationship was observed in either treatment group. Data for the 1.5 and 1100 ppm dose groups from Dawson et al. (1993) was republished and control data from other studies were pooled to conclude that rats exposed to levels of TCE >250 ppb during pregnancy have increased incidences of cardiac malformations in their fetuses. This is an inappropriate statistical practice.	A dose-response relationship does not require statistical significant at all tested doses. In the two highest doses of (Johnson et al., 2003) (originally published in (Dawson et al., 1993)), incidence of CHDs increases from 3.3% in controls to 5.5% in the lowest dose and 10.4% in the highest dose, a clear (albeit shallow) dose-response. EPA used data from all controls and dose levels in conducting BMD modeling to obtain a POD based on a selected BMR and model fit. Therefore, the original study NOAEL as determined by authors was not relevant for the Risk Evaluation.
79, 72	**PUBLIC COMMENTS:** Problems with the Johnson et al. (2003) dissection technique. • It requires fixation and manipulation, including immersion or flooding with a formalin-based fixative prior to examination, which can both shrink and stiffen fragile tissues, that may result in tissue damage. • The foramen ovale opening in the atrial septal wall poses a challenge	Any artifacts from this dissection technique would be expected to be equally observed across all groups since the investigators were blinded and required unanimous confirmation of defects. While (Fisher et al., 2001) did not report a statistically significant increase in defects, it did

	for examining the atrial septum before birth and supports why the recommended cardiac dissection methods in EPA guidelines do not require opening of the atria. • Some SACC members noted the dissection technique was also used in Fisher et al. (2001) which did not report a significant increase in fetal cardiac defects either with TCE, or with the metabolites, trichloroacetic acid (TCA) and dichloroacetic acid (DCA).	report observations of the same set of defects observed in (Johnson et al., 2003) (Table_Apx F-6). The lack of statistical significance in Fisher et al. (2001) from TCE treatment may be due to the elevated incidence in controls, which used soybean oil instead of water.
79	**PUBLIC COMMENTS:** Re. Johnson et al. (2005) EPA staff suggested to the SACC that, while none of the TCE exposure groups were tested at the same time, each exposure group did have a respective concurrent control group. • If there is evidence to support this claim, EPA has not shared this information with the public or the SACC. EPA's claim regarding the inclusion of concurrent controls is not supported by information presented by staff in their most robust analysis. Specifically, as illustrated in Makris et al. (2016), none of the start dates of the control groups align with any of the four TCE exposure groups over the 6 years the various studies were conducted prior to the publication. • If EPA has identified original records that contradict the timing of the studies by Johnson et al. described by Makris et al., these should be made public. The post-hoc pooling of controls across time, including studies that did not involve TCE exposures, artificially inflates the statistical power making it prone to false positives based on apparent statistical significance.	While control and treatment group experiments were not started or completed at the exact same time, there was substantial overlap in the timelines for many of the groups. EPA does acknowledge however that this is not standard practice and has included the issue as a significant limitation of the publication (see Table_Apx F-1).
79	**PUBLIC COMMENTS:** Johnson et al. (2003) provided no documentation to support the claim of a 35 percent reduction of TCE levels in drinking water over a 24-hour period or indicate whether that reduction includes loses during preparation formulations as well as from the water bottle during the 24-hour period. EPA's analysis of the TCE losses in Johnson et al. appears to have misinterpreted the study reporting; the percentage difference between the initial and average concentrations are identical for each of	EPA acknowledges this concern. In evaluation of Metric 7 for (Johnson et al., 2003), EPA states: "The rarity of obtaining almost identical measurements across doses is worth noting, however equal loss across dose groups mitigates concerns about dose-response, and may even suggest underestimation of toxicity depending

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	the dose groups, suggesting that the data reflect a general assumption about TCE losses rather than on empirical data. This concern should have been reflected in EPA's study quality evaluation and scoring for this metric.	on calculations."
76	**PUBLIC COMMENTS:** The major focus of previous TCE assessments (Makris et al., 2016) was on the presence of ventricular septal defects (VSDs) in fetuses. In the current risk assessment, EPA has shifted focus to emphasize atrial septal defects. Atrial septal defects were reported only in studies in which the fetal examinations were conducted by Dr. Johnson (Dawson et el., 1993; Fisher et al., 2001; Johnson et al., 2003). The occurrence of atrial septal defects in these studies appears to be sporadic. EPA studies (Smith et al., 1989; Epstein et al., 1992) on metabolites of TCE, that used the sensitive Wilson sectioning technique, found no ADSs. The Johnson atrial septal defects, therefore, are suspected to be an artifact. The Johnson dissection procedure and the presence of fixative may have displaced tissue in some samples, explaining why atrial septal defects only occurred randomly in a few embryos.	Any artifacts from this dissection technique would be expected to be equally observed across all groups since the investigators were blinded and required unanimous confirmation of defects. ASDs were observed in a dose-responsive manner in (Johnson et al., 2003), so the defects were not equally distributed across groups. In addition to differences in dissection method, defects that are inconsistently observed across studies may indicate variations in susceptibility between strains. Therefore, EPA has classified CHDs as a PESS concern and not necessarily likely to present in a large proportion of the general population.
95	**PUBLIC COMMENT** The draft risk evaluation places far too much emphasis rationalizing the validity of Johnson et al. leaving the impression that this is a useful study for risk characterization. The draft risk evaluation calculates risk estimates for fetal cardiac defects for each of the COUs based on the results from Johnson et al., despite concluding it would not be used to quantify risk. • The majority of SACC members determined that the quality of Johnson et al. study data as insufficient for estimating risks. • Several SACC members noted that EPA should have put more focus on the inhalation studies, since this route of exposure is of greater relevance to the exposure scenarios evaluated. • EPA should remove all the calculations of risk for fetal cardiac defects from the risk evaluation. Inclusion based on Johnson et al.	Inclusion of dose-response analysis from (Johnson et al., 2003) is not inconsistent with systematic review guidelines because it scored a medium in data quality and considered both weight of scientific evidence and statistical sensitivity of the data. EPA acknowledges that there is substantial uncertainty in the quantitative dose-response for CHDs and the relevance of these results to the human general population (Appendix F.1, Section 3.2.4.1.6, Section 3.2.5.3.1, and Section 3.2.6.1). Nonetheless, this endpoint is of concern to susceptible subpopulations (Section 3.2.5.2) and

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	study would be inconsistent with EPA's guidelines for systematic review and create confusion regarding EPA's conclusions about the risks of TCE exposure. • Only studies that are considered to be of sufficient quality under the systemic review guidelines should be carried forward to the risk estimation stage in the final risk evaluation.	consideration of dose responses from studies that are more sensitive than the more commonly observed responses observed among relatively young, healthy, and inbred laboratory rodent strains is important in accounting for human susceptibility. Therefore, the results from (Dawson et al., 1993) and (Johnson et al., 2003) were considered for dose-response analysis.
56	**PUBLIC COMMENTS:** The Dawson et al. (1993) study that reported on two TCE dose groups that were included in the Johnson et al. (2003) study had initially received a rating of High, but that rating was downgraded to Medium based on the study evaluator's professional judgment.	Thank you for your comment.
60	**PUBLIC COMMENTS:** EPA scored Johnson et al. (2003) as medium quality, although according to the guidance, the study would be unacceptable. This is indicative of inconsistency in conducting data quality assessments (*e.g.,* in this case, the study authors were contacted to obtain additional information not found in the published report, while in other cases, *e.g.,* Hardin/Beliles, studies were disregarded without even considering the full study reports).	(Hardin et al., 1981) did not show exposure-related findings for each study group and results were only briefly described in the text. Additionally, the study did not report how animals were allocated to groups. The original (Johnson et al., 2003) publication reports both blinding and random allocation to groups along with summary and defect-specific results for each group.
51	**PUBLIC COMMENTS:** Issues with study quality scoring for Dawson et al. (1993)/Johnson et al. (2003) • Metric 4: Scored "low", should be "unacceptable" for use of non-concurrent, pooled controls. • Metric 7: Scored "Med", should be "low" for inadequate reporting of preparation and storage of highly volatile test compound. • Metric 8: Scored "Med", should be "low" for uncertain TCE solution exposure concentrations and group housing of animals. • Metric 16: Scored "high", should be "low" for use of unvalidated,	Scoring for each of these metrics was based on consistent interpretation of the bins across all studies. In many cases, the scoring for a particular metric between bins is ambiguous, however the same interpretations were applied to all studies in the database.

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	non-good laboratory practice (GLP) dissection technique. • Metric 20: Scored "Med", should be "low" for uncertainties/deficiencies in control responses. • Metric 23: Scored "high" should be "low" or "unacceptable" for insufficient reporting of statistical methods and uncertain appropriateness. Overall: Scored "Med", should be "Unacceptable"	
51	**PUBLIC COMMENTS:** The result of EPA's biased review and selective and inconsistent application of TSCA study quality metrics is that EPA ultimately characterizes what is well-documented to be a clearly flawed, unreliable and irreproducible rat drinking water study (Dawson et al., 1993/Johnson et al., 2003) as a reliable study equivalent in study quality to a superior-designed, GLP study (Charles River, 2019/DeSesso et al., 2019) that followed the Organisation for Economic Cooperation and Development (OECD) Guideline protocols utilizing a validated outcome assessment technique.	The studies end up with the same scores however for different reasons. Following OECD Guidelines does not ensure a high score for data quality because data quality evaluations also take into account the purpose of the study and other considerations. While there is substantial uncertainty about the Johnson et al dose-response, Charles River 2019 suffers from inconsistency in data reporting, higher reported TCE loss, and indications of reduced sensitivity.
HSIA/CRL/DeSesso et al. (2019)		
64, 106, 108, 47, 99	**PUBLIC COMMENTS:** A study by DeSesso et al. (2019) singularly focuses on refuting the findings of Johnson et al. (2003) to argue that developmental exposure to TCE does not induce cardiac malformations. • Cardiac effects were identified, but study authors ignore them by erroneously deeming the observed effects to be insignificant. • EPA found the methodology was of reduced sensitivity, not a "close enough replication to Johnson et al. to sway the WOE for the endpoint on its own," and that the results do not entirely contradict the conclusions of Johnson et al. (2003). • DeSesso et al. does not negate the body of evidence supporting TCE-induced cardiac malformations, and itself presents methodological shortcoming and unsupported conclusions. • Even with its flaws, this study provides evidence of VSDs in the	The full review of (Charles River Laboratories, 2019) (publicly published as DeSesso et al. 2019) is contained in Appendix F.2 of the Risk Evaluation which discusses many of these considerations. EPA agrees that the CRL study does not refute the findings of (Johnson et al., 2003), however it was considered as slightly negative for strength and overall grade in the WOE analysis.

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	developing heart, supports the findings of the Johnson et al., and adds to the overall WOE for this endpoint. Authors dismiss these findings by proposing, despite evidence to the contrary, that these developmental defects heal over time "without adverse effects."	
78	**PUBLIC COMMENTS:** The CRL (2019) study does not negate the Johnson 2003 study and may support its findings. • The Oregon Health Authority (OHA) and Department of Quality (DEQ) disagree with the draft risk evaluation claim that the CRL (2019) study fails to reproduce the outcomes of the Johnson et al. (2003) study. • The CRL study did not adequately evaluate the range of heart defects (including atrial or valvular defects) in test or control groups as in the Johnson 2003 study. It also did not report on atrial or valvular defects in retinoic acid-exposed positive controls despite substantial literature indicating that such defects should have been evident following retinoic acid exposure. • The degree and direction of change among dose groups between the two studies was remarkably similar for VSDs. While the CRL (2019) study did not find a statistically significant increase in these defects when comparing each dose group against the control independently, it may have found a statistically significant trend had a trend analysis been completed and reported. • OHA and DEQ conclude that, to the limited extent to which the CRL (2019) study evaluated the same endpoints as the Johnson (2003) study, it may support, rather than refute, the Johnson (2003) study. The CRL study should not be used as justification to decrease EPA's confidence in Johnson et al. or the POD derived from it.	

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108, 99, 64	**PUBLIC COMMENTS:** In Appendix G of the draft risk evaluation, EPA recognized the limitations of the DeSesso et al. (2019) study. Specifically: • Retinoic acid (the positive control) was administered in a completely different manner than TCE (gavage on gestation days 6-15 vs. drinking water on gestation days 1-21), which calls into question the experimental design and compromises its validity. • The dissection method has reduced sensitivity and no report of valve defects (including positive control), and no examination of atrial septal defects. • DeSesso et al. (2019) attempted to downplay the significance of the small VSDs (<1 mm) that were observed in their study, claiming that "small VSDs which close spontaneously...should be considered normal developmental delay." Epidemiological literature indicates small VSDs can result in adverse effects and evidence does not support DeSesso et al.'s assertion that small VSDs do not have clinical significance. • The study was commissioned and supported by the HSIA and the American Chemistry Council (ACC), companies that have direct and substantial financial interests in the continued production and use of TCE as well as with respect to potential liability associated with releases and exposures to TCE, including from contaminated sites. There is a risk of bias.	
83	**PUBLIC COMMENTS:** It is not logical to take the chemical industry backed studies seriously when there are better, very thorough, long-term scientific studies available by unbiased, well-respected scientists. There needs to be non-chemical industry backed studies that genuinely refute the 2003 Johnson study before backing off on TCE regulations. These studies need to look at all types of fetal heart defects, not just a carefully selected few.	

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108	**PUBLIC COMMENTS:** Runyan et al. (2019) point out that DeSesso et al. utilized a static assessment methodology that captures only a subset of dysmorphologies and does not evaluate actual function and a study design that ignores the many studies published in the last 18 years that show TCE toxicity at exposures (*in vitro*) lower than 1,000 ppm, as well as evidence that TCE exhibits nonmonotonic effects. Runyan et al. (2019) argue that the conclusion of DeSesso et al. that ingestion of TCE in drinking water at less than 1,000 ppm does not cause heart defects is not supported by their own data.	
64	**PUBLIC COMMENTS:** The CRL study conducted a "targeted" analysis, so that it doesn't look at other developmental malformations, including some that were identified in the Johnson et al. study (*e.g.,* atrial septal defects). Thus, the CRL study was only a partial replication of the Johnson study because it didn't look at all effects; it was designed to be a negative study by not fully examining TCE-induced developmental malformations that are well-established in the peer-reviewed literature.	
64	**PUBLIC COMMENTS:** The CRL study argues that, based on published data, defects in the membranous septum tend to "resolve postnatally, without adverse effects on postnatal survival of the animals" and thus should not be considered adverse, referencing two rat studies to support this claim. There is another study in rodents, however, that indicates even small and seemingly healed chemically-induced VSD at birth "may permanently alter the capacity of the postnatal heart to adapt to pregnancy and this may have transgenerational effects." There are some supporting data for this same effect in people. There is no scientific basis to dismiss evidence of adverse effects.	EPA agrees with the commenter, and this claim by the CRL study (Charles River Laboratories, 2019) is rebutted in Appendix F.2.2.4.
99, 64	**PUBLIC COMMENTS:** The statistical analysis in DeSesso et al. is inappropriate. • The unit of analysis is the litter, but with only 20 litters, the analysis is likely to be statistically underpowered. Statistical analyses should	EPA agrees that a trend analysis would be better, however pairwise analysis is consistent with statistical methodology for other studies

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	be done using both the litter and the individual fetus. • The study primarily used pairwise statistics instead of trend analysis. A trend test would be preferable. • The use of two-sided tests is inappropriate; a one-sided test should have been done, which would increase statistical power and likely would have resulted in a study outcome showing statistically significant harmful effects of the treatment. • If the VSDs from this study on an individual animal basis are run through the Cochran Armitage trend test, the one-sided p-value is 0.0196, which is significant. EPA should provide this analysis, incorporating an adjustment for litter effect as appropriate, in Appendix G. • The study misuses statistics as a weapon to cut away evidence of adverse effects, rather than a tool to identify associations where they may occur.	including (Johnson et al., 2003). EPA chose not to perform dose-response analysis on the results of the (Charles River Laboratories, 2019) study because the methodology from (Johnson et al., 2003) was considered more sensitive and therefore the results of dose-response analysis from those results were used for POD derivation.
99, 64	**PUBLIC COMMENTS:** The CRL study misused historical controls. • The Charles River Ashland historical control data range for major heart vessel variations is 0.0 to 0.86% per litter. The study dismisses the major blood vessel variations by saying they are within the historical controls – in fact, they are not. The incidence at the high dose is 2X the historical control. • The HSIA's use of historical control data is pieced together after-the-fact (*post hoc*) from old publications from labs in China in the 1960s and early 1970s. Per EPA cancer guidelines, the most relevant historical data come from the same laboratory and the same supplier and are gathered within 2 or 3 years one way or the other of the study under review; other data should be used only with extreme caution due to genetic drift in the laboratory strains, differences in pathology examination at different times and in different laboratories (*e.g.,* in criteria for evaluating lesions; variations in the techniques for the preparation or reading of tissue samples among laboratories), and comparability of animals from different suppliers.	EPA agrees that the use of decades old post-hoc historical controls is not appropriate. It is unclear why the (Charles River Laboratories, 2019) study focused on the historical controls discussion at all, because it is not very relevant to the comparison with the Johnson et al. study. The Charles River methodology may have been highly sensitive to VSDs, and in fact the incidence of VSDs was very similar to that observed in Johnson et al. which used a novel sensitive dissection technique. The primary concern with the Charles River study is not the identified incidence of VSDs but the absence of many other defect types.

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	• The HSIA report applies a cherry-picked use of historical control data for some endpoints but not others, with no real rationale provided. This is inappropriate. The oscillation between using within-study and historical controls casts doubt on the rigor and consistency of the statistical analysis, making it appear instead to be manipulated and biased to dismiss evidence of harm. • The study reports that 2.4% of control fetuses developed VSDs. However, in Appendix 8, the incidence of various interventricular septal defects in the historical control database is recorded as 0.01% with a maximum mean incidence of 0.26%. DeSesso et al. (2019) comment on these differences, noting that "the mean litter proportion of VSDs in the control group was more than 9x higher than the maximum mean value for this parameter in the historical controls. The extreme discrepancy between the CRL concurrent and historic control incidence data is surprising and concerning. During the TCE SACC meeting, several panelists highlighted that this observation suggests that the animals used by DeSesso et al. (2019) represent an anomalous population. Overall, this inconsistency increases skepticism about the applicability and conclusions of this study and indicates that the findings should be interpreted with extreme caution.	
66, 34	**PUBLIC COMMENTS:** Had DeSesso et al. (2019) (supported by HSIA and ACC) been interested in objectively testing TCE and heart defects, they should have included ultrasound or other measures of cardiac function, changes in calcium homeostasis, examination of developmental gene expression, a more sensitive examination of morphology and a range of exposure that extended down to 5-10 ppb. All of these approaches have been developed since the report of Johnson et al. (2003) and are reported in the literature. It appears that the study was designed only to challenge Johnson et al. (2003) rather than to objectively test TCE effects on heart development. This study should be disregarded because of the bias in the experimental design and the bias identified by the funding source.	EPA has discussed limitations of the Charles River/DeSesso study (Charles River Laboratories, 2019), however it was still overall a relatively well-conducted study despite insufficiently addressing its stated goal of recapitulating the methodology of (Johnson et al., 2003). Therefore, it was considered along with all other relevant studies in the overall WOE analysis.

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64, 54	**PUBLIC COMMENTS:** It was proposed that EPA consider presenting a statistical analysis of the CRL data grouping the two reported cardiac malformations – the membranous interventricular septal defects and the cardiac major vessels variations – since the two tissues share the same embryonic tissue origin, the truncus arteriosus, and developmental deformities in the membranous septum and variations in the great vessels often present clinically together.	EPA chose not to perform dose-response analysis on the results of the (Charles River Laboratories, 2019) study because the methodology from (Johnson et al., 2003) was considered more sensitive and therefore the results of dose-response analysis from those results were used for POD derivation.
76, 72	**PUBLIC COMMENTS:** There were numerous problems with EPA's evaluation of the positive control data from the CRL study. • The evaluation was not done in a transparent manner: References were not provided for the 25 retinoic acid studies that were included; the doses, routes, and durations of exposure used were not provided and may be irrelevant to those used in the CRL (2019) study; the criteria used to include a heart defect in the analysis was not reported (*e.g.,* did findings have to be statistically associated with retinoic acid treatment or only observed at least once in an retinoic acid treatment group)? • The evaluation was done in non-mammalian species. Both zebrafish and chickens develop outside the material anima and may not be relevant to what occurs in rats. • Some findings were reported only in mouse/hamster and not rat. • No report on how many heart findings occurred in a single fetus. • 20/35 findings were seen in only a single retinoic acid study. Only 11/35 were reported in >2 studies. • In the evaluation, the category of early developmental defects included endocardial cushion defects and abnormal heart looping. This terminology is vague, and it is not clear what is meant by these terms as used by EPA. Those terms are not ones used by contract laboratories; related defects would have been described by CRL using terms included in other categories. Despite limitations, the evaluation shows that the retinoic acid positive	Exclusion of the 25 retinoic acid (RA) studies was an oversight that has been corrected in the final Risk Evaluation. Chicken and zebrafish studies were a minority of the total studies and were included as to avoid bias in presenting the results of the retinoic acid literature search. EPA acknowledges that there may be differences in the specific defects observed in these species, however they are both well-established models for studying developmental toxicity and cardiac development. Notably, atrial septal defects were observed in (Johnson et al., 2003) and 5 independent RA studies in hamster and rat. Multiple other defects observed in Johnson et al, 2003 were also observed in at least one RA study, all of which were on mammals (most on rats or mice). EPA has added a table to the final Risk Evaluation including all identified studies and a breakdown of defects observed (Table_Apx F-8). A summary of defects identified across all

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	control incorporated in the CRL study demonstrated adequate sensitivity of the model to detect heart findings due to treatment.	studies are provided in Table_Apx F-7 and Table_Apx F-9.
76, 72	**PUBLIC COMMENTS:** The DeSesso et al. (2019) study was conducted over a single period of time, using statistically robust group sizes, with all treatment and control groups run concurrently. Volatility of TCE was taken into consideration. Maternal toxicity was assessed through weighing of dams throughout gestation and reporting of clinical signs. Fetal weights and internal sexing were recorded in order to enable assessment of potential developmental delays or sex-specific findings. Data were evaluated using the litter as the experimental unit. Examination of fetal hearts was done using an approved standard method, and findings were confirmed by a fetal pathologist and an external teratologist. A toxicokinetic arm was included to verify internal doses. Using linear extrapolation from the highest exposure group to the lowest, estimated TCE exposures ranged between 25 ng/mL to 0.006 ng/mL. • This well-designed study that did not replicate findings of Johnson et al. (2003), and along with support from Fisher et al. (2001) and Carney et al. (2006), it provides strong support for the position that real-world drinking water exposures to TCE (MCL = 5 ppb) are unlikely to present biologically plausible risks of adverse cardiac development.	EPA agrees that the study was overall well conducted. This study is included in the WOE analysis for cardiac defects and considered along with all other relevant studies (*i.e.,* the reasonably available information).
51, 72	**PUBLIC COMMENTS:** DeSesso et al. (2019) made the detailed and extensive laboratory report publicly available, whereas deficiencies in reporting and documentation are evident in the journal correspondence and errata that followed Johnson et al. (2003) (Hardin et al., 2004; Johnson et al., 2004, 2005, 2014), showing obvious disparity in transparency and documentation between these two documents.	Deficiencies in the data reporting for (Johnson et al., 2003) are acknowledged in the Risk Evaluation, however these concerns were at least partially addressed in subsequent errata and communications.
76, 79	**PUBLIC COMMENTS:** EPA's criticisms of the CRL (2019)/DeSesso et al. (2019a) study on rats	

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	are invalid. • EPA incorrectly states that the examination of fetal hearts was limited to the ventricular septum. The standard operating procedure describing the methods used includes examination of the semilunar valve, interventricular septum, bicuspid valve, and walls of the atrium and ventricle. • EPA states that the study lost an appreciable amount of TCE, equivalent to that reported by Johnson et al. The lack of description in Johnson et al. calls into question the accuracy and methodology used to measure TCE. Conversely, the CRL study took steps to minimize volatilization or photolysis. Analytical and toxicokinetic measurements were performed to assure internal exposure had occurred and all data is well documented. • EPA suggested that the lack of statistically significant effects in the CRL study was due to a high incidence of findings in the negative control group. As discussed in DeSesso et al. (2019a), the higher incidence is considered to be a function of the detailed evaluations of the heart that were conducted. The CRL historical control database shows a lower incidence as expected because those studies were done involving a less-detailed examination of the heart and is similar to the Johnson et al. (2003) and Fisher et al. (2001) studies.	EPA did not state that the examination was limited to the ventricular septum, but that the methodology was likely focused to primarily identify those types of defects. The effort taken to minimize volatilization does not discount the fact that volatilization did take place, indicating that the analytical dosing was lower than the nominal dose and potentially reducing the relative severity of observed responses. As indicated by other public comments, the use of historical controls from decades earlier in unrelated studies are not very relevant for comparison to the current study.
79	**PUBLIC COMMENTS:** A commenter suggested that the statistical analysis conducted by CRL was inappropriate. In direct contrast to EPA's guidelines for developmental toxicity studies, the commenter suggested that the statistical analysis should have been conducted on a per-fetus, rather than a per-litter basis. • DeSesso et al. present the CRL study data on both a per-fetus and per-litter basis. The commenter also suggested that a trend analysis should have been conducted to evaluate the data instead of a pairwise comparison to increase sensitivity. • A SACC member noted that while no clear trend is evident in the	EPA acknowledges this comment. EPA did not consider the issue raised by the other commenter in our evaluation of the study.

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	CRL data, it would be difficult to assess the significance of a trend (should it exist) over the four orders of magnitude of exposures in the study (0.25 to 1000 ppm). The CRL study report notes that two-tailed statistical tests were conducted at both the 5% and 1% significance level, which should address the comment that the analysis lacked statistical power.	
51	**PUBLIC COMMENTS:** EPA argues that genetic drift could explain why none of the other eleven reliable TCE-fetal cardiac defect animal studies – including those designed to replicate their findings – have provided TCE-fetal cardiac defect evidence in support of the Dawson et al. (1993)/Johnson et al. (2003) study. • EPA has not provided any supporting citations that might provide corroboration for this theory. • GLP studies designed to examine TCE-fetal cardiac defect hypothesis were conducted within a few years of Johnson et al. (2003), and not 1-2 decades after. Would genetic drift occur over very short windows of time? • The incidence of common fetal cardiac defects (*e.g.,* VSDs) in control Sprague-Dawley rats has been shown to be consistent across multiple breeders located on multiple continents over several decades (DeSesso et al., 2019). Given this evidence, cardiac development is highly conserved across vertebrate species and unlikely to be affected by genetic drift.	Genetic drift is more likely to explain the increased sensitivity of the animals in (Johnson et al., 2003) vs (Dawson et al., 1993). However, differences in animal sources could explain varied responses from different experiments conducted at the same time because genetic drift would have been occurring for years or decades in those distinct populations prior to being used for the experiment.
51	**PUBLIC COMMENTS:** The published, Open Access version of the CRL study, provided to EPA, which addressed many, if not all, of EPA criticisms, was ignored during the assessment and scoring the quality of this study.	The peer-review published study (DeSesso et al, 2019, available at https://onlinelibrary.wiley.com/doi/full/10.1002/bdr2.1531) confirms EPA's assessment that the study was designed to be more targeted in its focus on VSDs compared to (Dawson et al., 1993).
51	**PUBLIC COMMENTS:**	

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	Issues with study quality scoring for CRL (2019)/DeSesso et al. (2019) • Metric 5: Scored "low;" should be "Not applicable" – positive controls are not required, a score was selectively given to downgrade this study. • Metric 16: Scored "low;" should be "high" for using validated GLP technique. • Metric 20: Scored "Med;" should be "high" for clearly reported responses in controls. • Metric 23: Scored "Med;" should be "high" for clearly reported and appropriate statistical methods. • Metric 24: Scored "Med;" should be "high" for data reporting in publication and supporting data in publicly available report. Overall: Was downgraded to "med" should be "high."	Scoring for each of these metrics was based on consistent interpretation of the bins across all studies. In many cases, the scoring for a particular metric between bins is ambiguous, however the same interpretations were applied to all studies in the database.
Fisher et al. (2001)		
108	**PUBLIC COMMENTS:** DeSesso et al. (2019) repeatedly points to the Fisher et al. (2001) study to support an assertion that TCE does not cause congenital heart defects. However, the Fisher et al. (2001) study has serious shortcomings in both its methodology and its characterization of findings that significantly reduce confidence in its conclusions, and these have been acknowledged by EPA.	EPA agrees with these comments and discusses the (Fisher et al., 2001) study in the Risk Evaluation. The Fisher study had an elevated negative control which diminishes the strength of its negative result, and it is cited in Appendix F.2 as evidence of (Charles River Laboratories, 2019) having a narrowly focused dissection and evaluation methodology.
66	**PUBLIC COMMENTS:** TCE is non-monotonic and produces cardiac defects most strongly at very low exposure levels. Therefore, the failure of the Fisher et al. (2001) study, which used gavage with high concentrations, to observe heart defects in their animals is consistent with emerging understanding of the mechanisms involved.	

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76, 72 106	**PUBLIC COMMENTS:** Evaluation of the Fisher et al. (2001) data, in which fetuses were examined using the Johnson dissection method, show that this method is no more sensitive than the fresh visceral dissection technique used in the CRL study for detecting cardiovascular defects. • Although EPA's specific language that the Fisher et al. (2001) study did not find a statistically significant risk is correct, the study did find an elevated risk, reporting that "[t]he rate of heart malformations ranged from 3% to 5% across the TCE, TCA, and DCA dose groups…on a per fetus basis. On a per litter basis, the rate of heart malformations for TCE, TCA, and DCA ranged from 42% to 60%." The risk for fetal cardiac defects may not have been statistically significant, but that is not the same as finding no elevated risk. • The high background incidence in the soybean oil control, as identified by both the study authors and again by EPA in this draft risk evaluation, likely resulted in less statistical power to detect the risk, leading to an underestimation of risk. EPA cites that Fisher et al. "identified a significant number of … defects that match those identified in (Johnson et al., 2003) and (Dawson et al., 1993) (including atrial septal and valve defects)," indicating that while the study may not have been entirely consistent with previous studies on the particular endpoint of fetal cardiac defects, it was in agreement on other defects, meaning it was not as contrary to the Johnson et al. (2003) study as certain parts of the draft risk evaluation indicated.	
94	**PUBLIC COMMENTS:** Failure to observe cardiac malformations in TCE, TCA, and DCA in the Fisher et al. (2001) study substantially challenges the conclusion that TCE in drinking water or by inhalation induces cardiac malformations. The Fisher et al. (2001) study should be given greater emphasis in the WOE as it provides important information showing that TCE metabolites do not plausibly cause fetal heart malformations in rats at doses higher than what would be considered a lethal or Maximum Tolerated Dose (MTD).	All assays relevant to potential cardiac toxicity from TCE exposure were given equal consideration in the WOE analysis. The (Fisher et al., 2001) study scored (0/-) for TCE and (-) for metabolites in the cardiac defects WOE analysis (Table_Apx F-11), indicating that it did contribute negative evidence toward the WOE for cardiac defects.

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94	**PUBLIC COMMENTS:** The EPA comment that the Fisher et al. (2001) 300 mg/kg-day TCA dose was "too low to rule out effects at higher doses" is a dosimetric red herring in that TCA maximum blood concentrations resulting from this dose cannot be plausibly attained from TCE administered in drinking water or by inhalation. Toxicokinetic comparisons indicate that the 300 mg/kg oral TCA dose used in Fisher et al. (2001) produced a maximum systemic blood concentration of TCA that far exceeded the maximum TCA blood concentrations resulting from 1,000 ppm TCE drinking water or 600 ppm inhalation exposures.	EPA agrees that this statement is not appropriate as written and it has been changed to "but only a single dose level was used."
Wikoff et al. (2018)		
108	**PUBLIC COMMENTS:** EPA missed key flaws in Wikoff et al. (2018) that should have reduced its confidence in the conclusions of that review. The review adapts the Office of Health Assessment and Translation (OHAT) Risk of Bias rating tool for human and animal studies to assess the internal validity of experimental animal and human evidence linking maternal exposure to TCE to fetal congenital heart defects. • The study authors state that they modified the OHAT framework to tailor it to the specific research hypothesis under study and took some of the 11 research questions/domains from OHAT and created "subdomains" that split out the combined criteria into multiple, separate considerations. This separation creates additional opportunities to highlight shortcomings of individual studies. It is not clear whether the subdomains are quantitatively considered equivalent to domains (not clearly described), but the visual effect on risk of bias heatmaps is that studies that perform poorly on individual subdomains appear to be of even lower quality than they would be if subdomains were retained as single domains per the OHAT risk of bias rating tool. • Using this rating scheme, the Johnson et al. (2003) study performs especially poorly. It would seem that Wikoff worked backwards from shortcomings in conduct/presentation of the Johnson (2003) to put	EPA agrees that (Wikoff et al., 2018) involved some subjective decisions, as do all WOE analyses, and the Risk Evaluation indicates how the Risk Evaluation's WOE analysis differs from (Wikoff et al., 2018). However, it was not the goal of the Risk Evaluation to dissect specific aspects of other WOE analyses, only to indicate why the conclusions may have differed. EPA's WOE analysis incorporated relevance, data reliability, and strength of response, while (Wikoff et al., 2018) only focused on Risk of Bias, a measure of data reliability.

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	more emphasis on the elements of the OHAT framework that would devalue that study and cause it to be discarded. • Wikoff et al. (2018) select a bias rating of "Probably High" that there is indirect evidence that non-treatment-related experimental conditions were not comparable between study groups without presenting evidence to support this. • Wikoff et al. (2018) unreasonably scored Johnson et al. (2003) as "probably high" for risk of bias due to the different cardiac evaluation methods used. The superiority of certain heart dissection methods was inappropriately asserted that led to an incorrect poor risk of bias for Johnson et al. (2003). EPA noted the Johnson method was sensitive and capable of detecting a variety of septal and valve defects, as well as atrial, ventricular, and other miscellaneous abnormalities (many of which were not observable using the methods employed by the 2019 CRL study). • The completed risk of bias tables were not available from the Wikoff study. This lack of transparency prevents EPA and the public from examining the bases and justifications for specific study ratings.	
106	**PUBLIC COMMENTS:** Study conclusions for Wikoff et al. (2018) likely underestimate risk due to lack of consideration of mechanistic data. • Wikoff's lack of consideration of mechanistic studies removes from its evidence base "*In vivo* animal studies in rats and chicks [which] have identified an association between TCE exposures and cardiac defects in the developing embryo and/or fetus (U.S. EPA, 2011e)" and "provided strong and consistent supporting information for effects of TCE and metabolites on cardiac development and precursor effects."	EPA states in the Risk Evaluation that (Wikoff et al., 2018) did not account for mechanistic data. The study also did not assess data on TCE metabolites.
Toxicokinetic data do not support developmental cardiac defects as an endpoint for TCE		
79	**PUBLIC COMMENTS:** A comparison of TCE toxicokinetics following drinking water, inhalation, and gavage administration provides strong evidence that parent TCE is an implausible source of potential fetal cardiac defects.	The presence of non-detects for TCA does not indicate that TCE is not a plausible teratogen. The sensitivity of the assay is an important

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	The absence of detectable levels of TCE in maternal blood in rats exposed to up to 1,000 ppm in drinking water in the CRL study is consistent with previous drinking water findings. In contrast, TCE would clearly have been present in maternal blood in the gavage study by Fisher et al. (2001) and the inhalation study by Carney et al. (2006), neither of which reported a fetal cardiac defect increase in offspring of exposed rats.	consideration and it is possible that TCE metabolites are toxic at very low doses based on results from (Johnson et al., 2003) and various mechanistic data (Appendix F.3.3.). EPA discusses the non-monotonic dose response of cardiac defects and presents data supporting the dose-response in Appendix F.3.3. This non-monotonic dose response in both apical and molecular responses may explain the differences in observed responses via different routes and unexpected results at varying doses. The WOE analysis assigned reduced relevance to metabolite studies partially due to considerations of dosimetry and uncertainty regarding toxicokinetics via different routes, however they still contributed consistent support to the positive weight of scientific evidence.
72, 94	**PUBLIC COMMENTS:** The statement by Makris et al. (2016) "[t]he evidence supports a conclusion that TCE has the potential to cause cardiac defects in humans when exposure occurs at sufficient doses during a sensitive period of fetal development" is at odds with toxicokinetic data. Analysis of TCE exposures and the peak concentrations of TCE and TCA in maternal blood or plasma from three routes of exposure shows: • TCE Non-Detects in maternal blood in drinking water studies (CRL and Fisher et al., 1989) indicate parent TCE is not a dosimetrically plausible teratogen as postulated by Johnson et al. (2003). • TCE is unlikely to reach the fetal heart from exposure via drinking water because of substantial hepatic first-pass metabolism, in contrast to routes of exposure involving oral gavage and inhalation. • Higher peak TCA plasma levels are achieved in the gavage and inhalation developmental toxicity studies (Fisher et al., 2001; Carney et al., 2006) reporting no increase in cardiac malformations compared to the drinking water study (Johnson et al., 2003) reporting cardiac malformations. An absence of cardiac malformations by these routes was not due to insufficient systemic TCE/TCA dosing. Oral gavage and inhalation routes failed to show an increase in fetal heart malformations, even at systemic doses that were considerably higher than can be achieved by the drinking water route; the findings of Johnson et al. (2003) cannot be a biologically plausible effect.	
72, 94	**PUBLIC COMMENTS:** EPA fails to incorporate toxicokinetic data showing minimal systemic concentrations after oral exposures. It is incomprehensible that EPA	

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	ignored toxicokinetics in its discussion of the developmental toxicity data on TCE and its metabolites, and thus biased its conclusions in support of the poorly designed and reported drinking water findings of Johnson et al. (2003).	
51, 68, 79, 95, 103, 94	**PUBLIC COMMENTS:** The claim that studies on TCE metabolites (TCE or DCA) provided the strongest evidence in the animal database supporting the TCE-fetal cardiac defect hypothesis is not accurate because the dose levels used in those studies was high. Extrapolating to equivalent TCE concentrations would result in lethal doses that would likely exceed the LD_{50} in rodents. • EPA's conclusions on the TCE metabolite studies contradicts EPA's TCA and DCA IRIS assessments. • In the TCE animal studies that measured the levels of metabolites in blood, it is clear that the levels of TCA are substantially lower than the doses that were associated with development of fetal cardiac defects in the metabolite studies cited by EPA. EPA failed to provide any quantitative perspective on dose plausibility on whether the low dosages administered in drinking water generate the necessary TCA and DCA tissue concentration supported by PBPK and metabolism modeling.	
94	**PUBLIC COMMENTS:** The draft risk evaluation states that "Both TCA and DCA were convincingly shown to produce strong dose-related cardiac defects in the Smith et al., 1992, 1989 studies." • EPA failed to put these studies into perspective for the TCE hazard assessment by providing an estimate of the TCE exposures that would be required to attain the same TCA or DCA blood levels where cardiac defects were observed.	
Mechanistic/*in vitro* data supports/does not support developmental cardiac defects as an endpoint for TCE		
108	**PUBLIC COMMENTS:** The Urban et al. (2020) systematic evaluation of mechanistic data is flawed and does not negate the strong body of mechanistic data supporting the link between TCE and congenital heart defects. The NTP-	EPA agrees that Urban et al. 2020 (available at https://pubmed.ncbi.nlm.nih.gov/32145346/) does not sufficiently discount the weight of

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	OHAT method for evaluating a study's internal validity (risk of bias), adopted by Urban et al. (2020), does not address mechanistic studies, nor does it have a formal, structured approach to evidence integration for mechanistic data as it does for animal and human studies. This is a misappropriation of the NTP-OHAT method.	scientific evidence for mechanistic studies. The study inappropriately applied TSCA systematic review data quality metrics, often assigning Unacceptable based merely on incomplete data reporting, often for metrics that were assigned N/A by EPA.
108	**PUBLIC COMMENTS:** It appears that Urban et al. (2020) had a desired conclusion in mind when reviewing mechanistic data regarding TCE-induced congenital heart defects. • All of the studies inappropriately disqualified provided mechanistic evidence of the linkage between TCE and congenital heart defects. • This study was supported by the ACC, which represents companies that have direct and substantial financial interests in the continued production and use of TCE and potential liability associated with releases and exposures to TCE. As a general matter, risk of bias from conflict of interest is an important consideration in conducting systematic reviews and it should be considered by OPPT.	
108, 66	**PUBLIC COMMENTS:** Urban et al. (2020) relied on the deeply flawed TSCA systematic review scoring method for evaluating study quality and to support integration of evidence across identified mechanistic studies. • The majority of experimental datasets (approximately 70%) were assigned a score=4 for at least one of the OPPT study quality metrics, indicating the data sets are unreliable for risk assessment. These exclusions are unwarranted. • Urban et al. raise issues of substance preparation and storage, data analysis and testing for potential cytotoxicity as the primary reasons for rejection of 16 studies that provide mechanistic support for the link that they challenge. Dr. Raymond Runyan indicated that proper handling of TCE is a convention in the field that did not require specification. This information could have been provided if the study authors had been contacted. • A study by Harris et al. (2018) was downgraded because T tests were	

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	used rather than analysis of variance (ANOVA) in the analysis. However, since the authors were not attempting to utilize multiple independent measures together, ANOVA was not necessary for the analysis. • Several studies were downgraded because they did not test for cytotoxicity. Most studies, however, were testing low concentrations where previous data had shown that there is no cytotoxicity at those concentrations and therefore, disqualification for this reason is inappropriate. • No attempt was made to contact authors of the disqualified studies, many of whom likely would have been able to provide the missing information.	
66	**PUBLIC COMMENTS:** The systematic examination of mechanisms in relation to TCE and congenital heart defects as performed by Urban et al. (2020) is distorted by a basic asymmetry of resources. There has been no national funding for research on TCE and heart defects since 2009. The Urban paper focuses on an adverse outcome pathway (AOP) that was identified 20 years ago. Newer data on alternative mechanisms has only been produced by very limited local funding and suggests the existence of additional mechanisms that need more analysis. In contrast, the ACC and HSIA spend more than $7 million each year lobbying to relax restrictions on the use of TCE and contracting consultants to write papers to perpetuate the controversy.	
66	**PUBLIC COMMENTS:** The Urban et al. (2020) paper suggests that the chick embryo may be uniquely sensitive to TCE because it has no protective maternal metabolism and there is no placenta in this non-mammalian model. However, a recent paper by Chen et al. shows that the non-monotonic regulation of HNF4a activity by TCE, previously identified in the chick, is also a component of low dose exposure in the mouse model.	There is substantial overlap in relevant pathways of cardiac toxicity among developmental models. Appendix F.3.3 discusses potential Modes of Action (MOA) and other mechanistic considerations that support the observed non-monotonic dose-response, and these are often observed in varied cell types.
32	**PUBLIC COMMENTS:** TCE has been shown to induce a biphasic response in transcription factor	

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	HNF4a in the developing heart in chick embryos and in mammals (*e.g.,* Chen et al., 2020). HNF4a and TCE are each also associated with liver cancer, kidney cancer and Parkinson's Disease. These pathologies may be variously related to loss of HNF4a activity (low dose TCE) or over expression of HNF4a (higher dose TCE).	While there is not strong evidence for any particular singular AOP, mechanistic evidence suggests that multiple mechanisms and MOA may be involved. The involvement of multiple mechanisms could also explain the diversity of the observed cardiac defects.
79	**PUBLIC COMMENTS:** One SACC member noted that the relevance of the mechanistic information cannot be critically evaluated until EPA has developed a mechanistic framework (*e.g.,* an AOP) for the cardiac effect. While Makris et al. (2016) suggest an AOP for a subset of fetal cardiac defects, Urban et al. (2020) noted that the mechanistic evidence in mammalian models either do not support, or contradict, the postulated AOP, and found no basis for supporting the validity of TCE as an agent capable of causing such effects.	
51, 68, 79, 95, 103	**PUBLIC COMMENTS:** The EPA conclusion that the mechanistic literature represented the strongest and most consistent line of evidence in support of the TCE-fetal cardiac defect hypothesis is in stark contrast with the conclusions of a systematic review (Urban et al., 2020) that focused on these studies. • EPA rationalized the discrepancy by stating Wikoff et al. (2018) did not evaluate any mechanistic data, which may explain the difference in overall conclusions between the two studies. • The study quality review and scoring methods of the TCE-fetal cardiac defect mechanistic studies reveal several critical oversights and inconsistencies that violate norms of systematic review. EPA has overstated the quality of the TCE-fetal cardiac defect mechanistic literature and the degree to which it can inform the TCE-fetal cardiac defect hypothesis. For example, three mechanistic studies examined both TCE and metabolites, so EPA counted these twice. • Overall, EPA's conclusions were surprising given the heterogeneity and inconsistency in findings between and within species.	EPA disagrees that there is heterogeneity and inconsistency among mechanistic studies. The vast majority of mechanistic studies demonstrated responses supporting induction of developmental cardiac defects. Additionally, the non-monotonic dose-responses observed in (Johnson et al., 2003) are in agreement with several studies demonstrating varied responses at low vs. high doses. While there is not strong evidence for any particular singular AOP, mechanistic evidence suggests that multiple mechanisms and MOA may be involved. The involvement of multiple mechanisms could also explain the diversity of the observed cardiac defects. EPA does agree that mechanistic studies are of reduced relevance compared to *in vivo* animal or human data, and this was accounted for in the WOE analysis.
76, 68, 95	**PUBLIC COMMENTS:** There are problems with the *in vitro* studies used by EPA to challenge	

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	the key conclusion of DeSesso et al. (2019) and suggest that TCE may exhibit low-dose nonmonotonic effects on cardiac development. • *In vitro* studies are not kinetically equivalent to *in vivo* exposures. Based on the toxicokinetic portion of the DeSesso study, blood (and assumed associated embryo concentrations) are *within* or *substantially below* the doses used in the *in vitro* studies. Other oral and inhalation studies (Carney et al., 2006; Fisher et al., 1989) also found negligible TCE blood concentrations with high dose exposures. • *In ovo* or *in vitro* studies are not physiologically representative of mammalian embryos. Exposures occur outside maternal organism; therefore, no maternal metabolism or retardation of transfer to the embryo occurs. • Most of the studies are hypothesis-generating by design. The transcriptomics datasets lack any cross-species gene pathway coherence. • The endpoints used (*e.g.,* changes in gene expression; alterations in the methylation of DNA; changes in calcium regulatory transcripts of calcium flux) have not been demonstrated to be causative of cardiac malformations. • The findings are not relevant to the assessment of potential cardiac teratogenicity in mammalian embryos. • Overall, EPA resorted to a non-systematic, narrative approach in which only those datasets suggesting a potential TCE-fetal cardiac defect association were highlighted, while contradictory datasets were ignored. This approach fundamentally violates basic systematic review methodologies.	The WOE analysis assessed biological plausibility and not quantitative dose-response, so the use of high doses was only considered qualitatively as contributing to the reduced relevance of the studies. (Harris et al., 2018) was included in the WOE analysis for the data on chick embryos. See the supplemental document *Data Table for Congenital Heart Defects Weight of Evidence Analysis* for full details on the evaluation of each study.
94	**PUBLIC COMMENTS:** The biological relevance of the *in vitro* studies cited is questionable due the use of enormously high doses. Even studies that EPA claims support a non-monotonic dose response, with effects seen at lower, but not, higher TCE doses, used doses either within or higher than the worst-case estimates for TCE blood levels in the CRL drinking water study. Since	

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	cardiac malformations were not increased in the CRL study, the conclusion that these low-dose effects seen in some of the *in vitro* studies are non-monotonic are without merit.	
51, 95	**PUBLIC COMMENTS:** EPA only scored each of the mechanistic TCE-fetal cardiac defect papers that it included in its evaluation as a single study despite having multiple experiments. • Harris et al. (2018) reported TCE effects in three different models: HepG2 cells, chicken eggs exposed *in ovo*, and chicken embryos exposed *ex ovo*. Each experiment should have been scored separately as they likely would have unique scoring responses. It is not clear which experiment EPA was focusing on for their scores. • EPA mischaracterized what is a series of "unacceptable" experimental datasets as a single "medium quality" study for their TCE-fetal cardiac defect WOE.	
51, 95	**PUBLIC COMMENTS:** EPA failed to apply both the data interpretation and cytotoxicity testing metrics to most of the relevant TCE-fetal cardiac defect mechanistic studies. In addition, EPA inconsistently applied the Blinding of Outcome Assessors Metric (#19) to the relevant mechanistic studies, scoring this metric for some *in ovo* studies (*e.g.,* Drake et al., 2006a,b; Loeber et al., 1988), but not others where subjective observations were being reported and it was thus clearly warranted (Rufer et al., 2010).	(Rufer et al., 2010) used non-subjective echocardiography for evaluating hearts in addition to multiple quantitative and qualitative measures. (Drake et al., 2006a; Drake et al., 2006b) and (Loeber et al., 1988) focused on more subjective measures, and (Loeber et al., 1988) indicated blinding for researchers.
51	**PUBLIC COMMENTS:** EPA erroneously applied the *in vitro* study quality metrics to Collier et al. (2003), which is an *in vivo* study. This resulted in a faulty study quality score. Had the appropriate quality metrics been applied, this study would have been scored as "unacceptable" because it used an insufficient number of animals per dose group and did not report any statistical analysis of their findings.	Exposure occurred *in vivo*, however the experiment involved genomics of exposed fetal embryos. Statistical analysis is included as a metric in the *in vitro/mechanistic* criteria and was accounted for in the evaluation.
EPA WOE approach and conclusions for cardiac developmental defects		
SACC	**SACC COMMENTS:** It appeared to the Committee that the WOE assessment and the	This comment incorrectly interprets the role of

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	systematic review process used two different rating systems, despite having overlap in their goals and methods. Figure 3.3 explains that data interpretation is part of the systematic review process. This suggests that the draft risk evaluation should not need a separate WOE method, and the WOE discussion should be considered part of the scoring and integration components of the systematic review. The systematic review appropriate for dose-response would be included.	data quality as part of the systematic review process. Data quality is only one factor in considering data integration of the reasonably available data, which accounts for the weight of scientific evidence and must incorporate both relevance and strength of study results.
SACC	**SACC COMMENTS:** Recommendation: Revise the WOE to integrate strength and relevance of all *in vivo* animal and epidemiological study findings with available mechanistic evidence.	The WOE analysis already accounts for relevance and strength of all relevant studies, in addition to data quality (reliability).
SACC	**SACC COMMENTS:** Recommendation: Reconsider the scores assigned to the epidemiological evidence for TCE-induced cardiac anomalies. • Several Committee members felt the epidemiological data showing suggestive evidence of an association between TCE exposure and cardiac effects in offspring were weak. For example, none of the three studies showing positive associations (Brender et al., 2014; Forand et al., 2012; Wright et al., 2017) accounted for the residential location of the mothers during the critical period for cardiac development (3rd to 8th week of pregnancy) or had TCE exposure data for the study population. Instead, they all used the maternal location at the time of birth. Other weaknesses were noted as well. • Some Committee members thought that the relevance score of ++ given to Brender et al. (2014), Forand et al. (2012) and most of the other epidemiological studies in the WOE evaluation was too high, because they felt that it would be difficult to use the data from any of the three studies in question to develop a toxicity value, even though animal to human extrapolation is not needed.	There is some uncertainty in the exposure domains due to the lack of individual level exposure assessment, but the environmental monitoring procedure was well done. If the 22-32% of women are estimated to move during pregnancy, then 68-78% are in the same location during pregnancy, which would include the critical period for cardiac development. So, this was accounted for in the study. Potential for misclassification is accounted for in the reliability score of each study (+) instead of (++). Forand et al., 2012 - As the author also pointed out, this move would be true of both cases and controls. So, this is a non-differential misclassification which would bias the estimate towards the null (*i.e.,* resulting in an underestimate in risk). The sample size was indeed small, but still sufficient enough to see biologically relevant and statistically significant

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		differences in this population. Brender et al., 2014 - These limitations are already accounted for in the reliability score of the study. Wright et al., 2017 – Maternal location is not the ideal method and exposure misclassification is possible, but that's why the authors used a categorical exposure measure in the analysis (rather than continuous). It's easier to have confidence that particular households were placed in the right exposure group, despite the averaging that occurred by sampling location. There is no reason to believe that the results are unreliable.
SACC	**SACC COMMENTS:** Recommendation: Multiple *in vivo* animal TCE inhalation studies reporting no heart defects need more consideration in the WOE analysis of animal data. • Cardiac developmental anomalies have not been described in any of six TCE inhalation studies in rodents. Patterns in available developmental inhalation studies should be searched/assessed for specific endpoints to determine coherence. Particular attention should be paid to the study by Carney et al. (2006). Several Committee members said the draft risk evaluation needs to consider the findings of this study and others by Beliles et al. (1980), Cosby and Dukelow (1992), and Narotsky et al. (1995) in its WOE analysis. It was noted that Watson et al. (2006) published an analysis that concluded there was no causal association between TCE exposure at environmentally relevant concentrations and congenital heart defects. • For this draft risk evaluation, it appears data for the inhalation route would be preferred because inhalation exposures are most relevant to	EPA incorporated all relevant studies identified in previous assessments into the WOE analysis. Some studies were excluded because there was no evidence that they specifically examined cardiac defects. (Cosby and Dukelow, 1992) did not investigate heart defects, neither did (Narotsky et al., 1995). The only evidence of any heart investigation in (Beliles et al., 1980) is gross discoloration observed in dams. Watson et al. 2006 (available at https://www.sciencedirect.com/science/article/pii/S0890623805001759?via%3Dihub) is a review paper that was published well before many of the later studies incorporated into EPA's WOE analysis. These and other excluded studies are now cited in Appendix F.3.1.

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	COUs. As a result, findings from studies based on the inhalation route of exposure offer less uncertainty on POD estimates. PBPK models are useful; however, they do add uncertainty when conducting route-to-route extrapolation; hence, data from inhalation exposures and oral exposures are not equivalent. There are several high-quality developmental studies conducted with inhalation exposures. It is recommended that the risk evaluation focus on these (but not ignore the oral studies).	EPA relies on the peer-reviewed PBPK model and considers all routes similarly relevant, however EPA acknowledges uncertainties associated with route-to-route extrapolation in Section 3.2.6.2.
51	**PUBLIC COMMENTS:** EPA failed to include three oral TCE developmental toxicity animal studies – Cosby and Dukelow (1992); Narotsky et al. (1995); Narotsky and Kavlock (1995) – that are of medium quality and thus reliable for inclusion in the draft TCE-fetal cardiac defect WOE. Notably, none of these studies observed fetal cardiac defects associated with gestational TCE exposures, findings that impact EPA's WOE conclusion for animal studies.	
SACC	**SACC COMMENTS:** Recommendation: Improve the discussion on the MOA for TCE-induced fetal cardiac defects and identify gaps in the AOP that need to be filled. • The EPA's WOE approach to scoring evidence for cardiac defects was considered by the Committee to be overly simplistic and problematic, in that in the Committee's view, it gave more weight to incomplete mechanistic data than to *in vivo* animal evidence. • Mechanistic data are valuable in understanding MOAs and assessing biological plausibility. These data, however, are limited for TCE in that they primarily involve enzymes and gene induction. Metabolomic and proteomic evidence was not described. • The draft risk evaluation did not integrate and organize the mechanistic data into a coherent causal pathway from initial exposure to adverse outcome. The MOA narrative in the draft risk evaluation proposes several hypotheses for potential MOAs but concludes that the evidence to date does not identify a specific MOA. Why then are mechanistic studies assigned a score of '++' in view of	EPA has downgraded the summary score slightly for mechanistic studies from ++ to +/++ based on the absence of a single, clear AOP. EPA believes however that there are multiple contributing MOA for TCE's impact on cardiac defects. EPA already accounted for reduced relevance of mechanistic studies in the WOE analysis scores.

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	limited information and no apparent/likely mechanism? • The use of high-dose experiments in in vitro and avian systems limit their relevance in assessing risks of environmental TCE exposures.	

60, 52	**PUBLIC COMMENTS:**
	The approach for data integration and WOE assessment for hazard ID was not consistent within the TCE draft risk evaluation; the step was either absent (all endpoints except one) or conducted with a novel approach designed and implemented only for fetal cardiac defects.
	• An independent assessment of the overall WOE was not conducted for any of the endpoints other than fetal cardiac defects. That is, an independent, structured evaluation of the WOE was absent for the all endpoints considered except one. This is contrary to standard systematic review practice.
	• For all of the endpoints without a WOE evaluation, EPA relied on conclusions from previous authoritative assessments. This introduces uncertainty given that the assessments relied upon were not conducted using systematic review, nor were the WOE conclusions determined in previous assessments clearly described in the TCE draft risk evaluation.
	  o The EPA cites that no new data were identified to alter the conclusions of such, but presents no clear documentation of all of the studies that were considered "new" relative to the WOE conclusions being relied upon for each endpoint.
	  o Further, EPA conducted data quality assessments for studies related to these endpoints where a WOE was not conducted – a significant use of resources – exercises that largely seem to be unused given that an independent WOE was not conducted.
	• A *de novo* WOE approach was designed and implemented only for fetal cardiac defects. The approach was not part of EPA's Draft TSCA's Systematic Review guidance, nor has it been applied to any other chemical. The draft risk evaluation does not provide sufficient detail to evaluate the rigor and validity of the methods, and there were no opportunities for peer review. The two pages of bulleted
		The detailed WOE analysis was only performed for cardiac defects because that endpoint involves a large database of conflicting results. For other endpoints, the database is relatively consistent in favor of a weight of scientific evidence for that endpoint with very little conflicting evidence. Therefore, only a short summary of the newer studies was discussed for how they contributed to or countered the previous weight of scientific evidence established in the published 2014 TCE Risk Assessment. All studies published after the 2011 IRIS Assessment in addition to any key studies from the IRIS Assessment considered for dose-response analysis were evaluated for data quality and described in the Risk Evaluation.
		
		New studies identified in the literature search are identified in *Trichloroethylene (CASRN 79-01-6) Bibliography: Supplemental File for the TSCA Scope Document,* EPA-HQ-OPPT-2016-0737)
		
		The cardiac defects WOE analysis is based on existing methodology from the EPA Risk Assessment Forum (U.S. EPA, 2016i). It adds important considerations of data integration, relevance and strength, to the data quality considerations that were imparted by the

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	explanation provided are insufficient to understand or reproduce the WOE assessment as presented in the draft risk evaluation.
	• The data quality assessment and WOE evaluation methods rely partially on the same criteria and thus studies are evaluated using the same criteria multiple times – but with different results. This equates to "double counting" of criteria, which favors reviewer bias and is not consistent with the fundamental tenets of systematic review.
	  o It is difficult to remedy the rationale that the data evaluation metrics from the systematic review guidance would be used differently for evaluating the utility for dose-response and also for potential consideration in the WOE assessment (which seems "backwards" if the study has already been evaluated for utility in dose-response).
	• The *de novo* WOE approach applied to fetal cardiac defects utilizes subjectively assigned overall "scores" based on reliability, relevance, and strength – aspects that are not fully in alignment with traditional systematic review approaches.
	  o It is not clear if this approach considers aspects commonly evaluated as part of determining the certainty or confidence in a body of evidence in systematic review or those commonly assessed in causation analyses.
	  o In particular, an evaluation of the biological plausibility of a response *in humans* should be assessed; this is not well-defined in the WOE approach and is critical to the topic to which it is applied given that much of the mechanistic data are in non-mammalian models and are in contrast to findings observed in mammalian studies.
	  o The individual scores for reliability, relevance, and strength are subjectively assigned, as is the overall score for each type of evidence. The overall score appears to employ weighting by evidence stream, though the description of this method is not sufficient such that it can be reproduced. It is not clear what the overall score means in terms of hazard characterization – *i.e.,* is it
		systematic review data quality evaluations. EPA acknowledges that the systematic review guidance for the first 10 Risk Evaluations did not explicitly describe a process for data integration, however EPA is working with the National Academies of Science to develop a more robust process for the future that may incorporate principles of this WOE analysis.
		
		While expert judgment is part of any WOE analysis, scores for each study and domain were consistently applied across all studies. The methodology and scoring guidance are presented clearly in Appendix F.3.1. The overall result indicates the relative support for an association of TCE exposure with cardiac defects. It supports that TCE exposure is more likely than not to increase risk of cardiac defects. It does not determine the dose-response of the endpoint or any quantitative assessment of the POD.
		
		The SACC did peer review the WOE analysis as part of the overall Risk Evaluation and this analysis has been updated based on public comments including this comment. It is based on existing methodology from the EPA Risk Assessment Forum (U.S. EPA, 2016i). The reliability metric was evaluated with the TSCA systematic review data quality evaluation in mind, but with a more focused evaluation of data quality for the particular outcome at hand. The reliability scores closely track the TSCA systematic review data quality scores for all

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	a measure of the magnitude of a potential association? Is it confidence in an effect? The meaning of the overall score should be defined. The output of the WOE assessment should be further connected with the risk evaluation process, particularly as it relates to the differential approaches for individual study assessment and the requirement to utilize individual studies to develop PODs for purposes of the risk evaluation.	studies. EPA acknowledges that the systematic review guidance for the first 10 Risk Evaluations did not explicitly describe a process for data integration, however EPA is working with the National Academies of Science to develop a more robust process for the future that may incorporate principles of this WOE analysis. The methodology and scoring guidance are presented clearly in Appendix F.3.1.
106	**PUBLIC COMMENTS:** EPA has employed a *post hoc* WOE analysis based on a hierarchy of preferences against one single endpoint only. • The *post hoc* method is unvalidated, not empirically based, has not been subject to peer review nor public comment, and falls short of the best practice methods in systematic review methods, which is the codified approach that EPA must take for risk evaluations. • For example, for the metric of reliability, instead of looking at the overall study quality evaluations already completed by EPA for TCE, as would be normal practice when assessing the influence of risk of bias on the quality/certainty of a body of evidence, EPA performed a separate evaluation focused on "key attributes." This is inconsistent with how the quality of the evidence should be evaluated based on the overall risk of bias of the included studies. Additionally, EPA is not clear in its definition of these referenced "key attributes," lead to a higher score for metrics such as reliability. • There is no empirical basis for the "grades assigned based on the number and nature of the specific deficiencies identified." EPA has continued its pattern of creating a method that is incompatible with best practice, *post hoc*. EPA has not rated the confidence in the body of evidence in any of the draft risk evaluations that it has completed to date, nor has it implemented a predefined evidence integration step to come to its final conclusion on whether the chemical being assessed poses an unreasonable risk for certain COUs. Therefore, how EPA translates the available evidence into its final conclusion is unclear and unjustified by	

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	EPA. We strongly recommend that EPA use the validated, peer review method of NTP OHAT, which is consistent with best practice, for the evidence integration step in all risk evaluations it conducts. This method will allow EPA to transparently demonstrate the process for how the conclusions are reached in assessing human health hazards for each end point it assesses.	
108	**PUBLIC COMMENTS:** EPA adopted the methodology described in Risk Assessment Forum's WOE in Ecological Assessment to apply the evidence base for congenital heart defects, but uses a narrative summary in developing a WOE evidence for all other endpoints. • EPA fails to adequately explain/justify the selection of this particular methodology. • It is unclear whether EPA intends to apply this method in future risk evaluations, and the extent to which EPA considered more prominent GRADE-based structured frameworks for evidence integration used by analogous chemical assessment approaches (*i.e.,* National Toxicology Program OHAT health effects evaluations, University of California at San Francisco [UCSF] Navigation Guide, EPA IRIS assessments). EPA highlights the strength criterion as a distinguishing feature and explains that the strength of a given piece of evidence corresponds to its "magnitude, dose-response." There is concern that the inclusion of effect "magnitude" as a criterion for consideration could be interpreted as the fraction of the affected population, or the effect size of the change in a measure of outcome. An effect with a small "magnitude" either may affect a considerable fraction of the exposed population or could be sufficiently severe to warrant concern. Caution is advised in discounting evidence from well-designed, relevant studies with a small magnitude.	
108	**PUBLIC COMMENTS:** In the WOE analyses for congenital heart defects, EPA jointly considered the evidence for oral and inhalation studies in animals. When considered independently, the oral studies had an integrated area score of	The WOE analysis considered overall plausibility and likelihood of TCE exposure leading to developmental cardiac defects. While

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	(+), whereas the inhalation studies had an integrated area score of (-). Taken together, EPA assigned the *in vivo* studies via all routes a (0), which impacts the overall evidence integration for the endpoint (the quantitative nature of its impact is unclear for this semi-quantitative integration approach). However, it is not appropriate to consider the oral and inhalation routes together in this approach. Given potential differences in toxicokinetics and metabolism across routes, it is plausible that oral exposures are associated with the endpoint while inhalation exposures are not. EPA should conduct the WOE analyses separately by route. Then the *in vivo* animal toxicity studies score would have been higher (for oral exposure), which would have likely increased the overall Integrated Area Score and summary score.	EPA agrees that there may be differences via different routes, evidence via different routes together contribute to the overall WOE. It would be difficult to parse apart specific exposure routes via animal studies when combined with epidemiological and mechanistic data that are not necessarily route-specific.
51	**PUBLIC COMMENTS:** The framework used by EPA to integrate the mechanistic data into the larger WOE skips a critical step after study quality scoring: EPA fails to integrate the evidence *within* the mechanistic database – *i.e.,* bringing it all together to determine the degree to which it is able to provide a coherent story supportive of the biological plausibility of the TCE-fetal cardiac defect hypothesis and how it all fits together. Urban et al. evaluated three approaches for mechanistic data integration: • Hazard-based: Does the mechanistic evidence on its own suggest that fetal cardiac defects are a potential hazard associated with gestational exposures to TCE? • AOP-based: Does available mechanistic evidence inform the biological plausibility of TCE-fetal cardiac defects? • Risk-based: Do any of the mechanistic studies provide a dose-response dataset that should be considered as candidate studies in developing toxicity values?	EPA provides a summary of the mechanistic database both within the WOE analysis itself (Appendix F.3.2) and in a separate subsection (Appendix F.3.3) which discusses potential modes of action.
51, 68	**PUBLIC COMMENTS:** EPA's study quality and WOE evaluations for the TCE-fetal cardiac defect hypothesis contain several errors and examples of inconsistencies in how EPA interpreted and applied its study quality metrics across the various evidence bases (human, animal, mechanistic), as well as bias in	EPA applied data quality metrics consistently to all studies evaluated in the Risk Evaluation, however interpretations may differ for similar studies based on the available information. Some

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	several key inter-study critiques. There is a noticeable discrepancy in the level of detail and latitude given studies of the mechanistic and human evidence base relative to the animal studies, suggesting a problematic variation in the level of reviewer expertise between these databases that appears to result in deference to the former at the expense of the latter. The draft risk evaluation: • Inconsistently applies study quality metrics between studies. • Fails to apply all relevant study quality metrics (*e.g.,* data interpretation, cytotoxicity metrics for *in vitro* assays). • Re-scores initial study quality results using a process outside of the prescribed systematic review protocol and based on subjective judgment (introducing subjective bias into the evidence base). • Inconsistently follows up with study researchers (introduction of subjective bias into the evidence base). • Excludes relevant TCE-fetal cardiac defect studies from the assessment (unexplained exclusion criteria).	metrics were scored as N/A if they were only required for certain study types/assays. As stated in Appendix F.3.1, "This analysis was performed in parallel with the systematic review data evaluation of the individual studies. The WOE analysis had a greater focus on relevance to the specific endpoint while the data evaluation metrics aimed to evaluate the utility of a study for dose-response analysis." Usually scores were aligned between the data quality and WOE reliability scores. EPA has added the list of excluded studies to Appendix F.3.1 based on no indication of direct assessment of cardiac defects. As stated above, all metrics may not be applicable for all studies. The metric for cytotoxicity was primarily applicable for study types in which it is required by OECD guidelines (*e.g.,* Ames assay for genotoxicity). Expert judgment is considered in all data quality evaluations when the metrics do not fully capture the full scope of a study's data quality. EPA opened communications with authors of both positive (Johnson et al., 2003) and negative (Charles River Laboratories, 2019) studies in an attempt to clarify missing or unclear information.
51, 68	**PUBLIC COMMENTS:** There is evidence of reviewer bias in the systematic review process. Consistent scoring was not applied to studies that did not report test substance source (Metric 2). • Two key *in vivo* studies were scored as "not rated/not applicable" for Metric 5, but this metric was removed from scoring for all other animal and mechanistic studies. The discrepancy was not justified. • Metric 19 was scored in less than half of the applicable studies. • Metric 23 "scoring and/or evaluation criteria" were scored as "not applicable" for *in vitro* studies without justification. • EPA only scored Metric 24 "cytotoxicity testing" in one cell culture study while excluding it from study quality scoring for all other *in vitro* experiments. All of those not scored did not report cytotoxicity testing. • There were several instances where study scores were overturned by an evaluator based on subjective judgment, where the rationale did not adhere to any framework or protocol decision making tree.	

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	• There was subjective bias (in favor of studies supporting a WOE for cardiac defects) in which studies correspondence with authors was cited as supporting evidence for metric scores.	
51	**PUBLIC COMMENTS:** Lack of quality control measures during systematic review introduces additional uncertainty into what is already a highly subjective and questionable WOE evaluation process, further calling into question EPA's attempt to integrate the TCE-fetal cardiac defect evidence streams.	All studies were evaluated by two reviewers to ensure consistency among scoring. For the WOE analysis, all criteria and summary scores were additionally reviewed for consistency among studies and domains.
51, 95, 94	**PUBLIC COMMENTS:** EPA concluded that "[O]verall, the *in vivo* animal toxicity studies provided mixed, ambiguous evidence for an effect of TCE (summary score of 0)." This conclusion is a mischaracterization of the animal data. With the exception of Dawson et al. (1993)/Johnson et al. (2003), the database is comprised of high-quality studies, with relevant routes of exposure, that failed to demonstrate any association between *in utero* TCE exposure and fetal cardiac defects. EPA dismissed an inhalation study by Carney et al. (2006) that perhaps provides the most definitive data on the fetal cardiac defect endpoint, because it uses the most relevant exposure route and underwent a rigorous peer review process by multiple federal agencies, including EPA, and was given a high quality data score. The disregard of Carney et al. (2006) points to a bias in EPA's approach to evaluating the developmental data rather than supporting an agenda based on the WOE.	EPA did not dismiss the (Carney et al., 2006) study. The Carney study scored (+++) for reliability, higher than any other TCE animal study. It is included in the WOE analysis and EPA states that "the summary score for the inhalation studies was (-), primarily driven by the weight of the (Carney et al., 2006) data but reduced by the weaknesses of the other studies and the limited number of acceptable studies with non-ambiguous results."
51	**PUBLIC COMMENTS:** The Galba et al. (2012) study is scored as a "High Quality" study; however, EPA erroneously characterize it as a "Medium Quality" study in the WOE spreadsheet, without providing justification. This impacts the human WOE determination because this is a negative study of high quality, so the unjustified downgrade in study quality reduces its impact on a weak dataset.	EPA assumes that the commenter is referring to (Gilboa et al., 2012). EPA appreciates this comment, there was a mistake in the data table for the WOE analysis. The study has been updated, and the reliability score has been raised to +/++, with some remaining limitations due to potential exposure misclassification. This change in reliability score does not affect the

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		overall grade, which is dictated by the lowest magnitude of the three scores for reliability, strength, relevance (strength was scored (-)).
51, 68	**PUBLIC COMMENTS:** Wright et al. (2017) was purportedly scored an initial "High Quality," but was then downgraded to "Medium Quality" for issues of directness (*e.g.,* investigating proximity to TCA and DCA, rather than TCE). However, this study quality downgrade was ignored in the WOE, where this study was rated as the only high reliability study in the dataset.	As indicated in *TCE Data Table for Congenital Heart Defects Weight of Evidence Analysis*, the study was downgraded in the TSCA data quality evaluation because TCE was not directly evaluated, however the reliability is still high when fit-for-purpose of evaluating TCE metabolites. As with Gilboa et al. 2012, the overall grade was dictated by the lowest score (strength and relevance were both scored (+)).
51	**PUBLIC COMMENTS:** EPA over-characterized the outcome strength of the findings of the Brender et al. (2014) study, which reported weak associations between proximity to TCE and select fetal cardiac defects. EPA did not reflect these weak findings in its rating (positive, or "+" vs. weakly positive, or "0/+").	The finding was statistically significant, despite the modestly increased OR. Therefore, the study was scored (+) for strength, as opposed to (0/+) which suggests ambiguity.
51, 72	**PUBLIC COMMENTS:** The CRL study is consistent with the negative TCE-fetal cardiac defect findings that have been reported in 11 other animal studies (oral and inhalation), all of which can be characterized as reliable per TSCA study quality scoring. The Johnson et al. (2003) positive findings remain a unique outlier in this evidence stream that can reasonably be explained by the many underlying issues in study design and reporting. EPA does not properly account for multiple robust apical developmental toxicity studies that show no increase in heart defects and ultimately minimized the negative TCE-fetal cardiac defect animal studies (comprising all but one of the studies in the animal database) while enhancing the single, relevant positive animal study.	All studies are considered equally for their contribution to the WOE analysis. While (Johnson et al., 2003) and (Dawson et al., 1993) are the only positive animal studies on parental TCE, there are several positive studies on TCE metabolites that contribute to the overall WOE.
51	**PUBLIC COMMENTS:** Twelve animal studies demonstrate a lack of association between *in*	

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	utero TCE exposure and fetal cardiac defects, including all inhalation studies, representing the most relevant route of exposure for the human exposure scenarios evaluated in the TCE draft risk evaluation. The TCE-fetal cardiac defect animal data do not support the TCE-fetal cardiac defect hypothesis.	
60	**PUBLIC COMMENTS:** POD for the cardiac endpoint is based on a single study; there are 12 others reporting lack of effect. The POD selection metrics do not address negative findings in selecting the POD for an endpoint.	
51, 72	**PUBLIC COMMENTS:** There is concern about dependence on a single flawed study to conclude that TCE exposure may cause fetal heart malformations, despite evidence to the contrary from multiple, well-conducted studies. EPA's interpretation of the cardiac data has had a profound effect on the remediation of contamination sites. • Follow-up studies by Fisher et al. (2001) and DeSesso et al. (2019) did not observe cardiac defects despite repeating as many aspects of the original study as possible. EPA has offered an expanding list of possible explanations – exposure route specificity, importance of mechanistic data, genetic drift, possible role of metabolites, and most recently, differences in the dissection techniques. The problems with EPA's consideration of the cardiac defect data can be seen in several aspects of the draft including inconsistent application of the TSCA systematic review, mischaracterization of the quality and reliability of the available cardiac mechanistic literature, failure to relate the levels of metabolites required to cause heart effects in rats with the levels generated from typical TCE exposures, and clear evidence of bias in the consideration of the WOE for cardiac effects.	EPA disagrees with the characterization of EPA's WOE determination. There are multiple lines of evidence in support of an association between TCE exposure and cardiac defects. However, EPA acknowledges that while there is qualitative support for the endpoint, based on uncertainties in the dose-response for this endpoint and other considerations EPA has selected immune endpoints as the best overall endpoints for risk conclusions (Sections 3.2.5.4.1, 3.2.6.1.1).
103	**PUBLIC COMMENTS** EPA did not fully consider and integrate all of the relevant literature in its systematic review of the developmental evidence. EPA paid little attention to other reproductive/developmental studies that did not observe increased fetal cardiac malformations. EPA must also adhere to	EPA considered all relevant studies identified in either previous WOE assessments or the TSCA literature search. EPA has added a list of studies excluded as off-topic to Appendix F.3.1. EPA

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	systematic review principles that when followed (as shown in the Wikoff et al., 2018 and Urban et al., 2020 papers), reject TCE as a proven cause of fetal cardiac malformations.	followed systematic review principles, which include data integration in addition to data quality.
103	**PUBLIC COMMENTS** It is not clear why EPA presented a hazard and toxicity value assessment that emphasized the Johnson et al. (2003) study when in the draft determination, EPA elected not to use the reference dose based on Johnson et al. (2003). EPA should adjust the WOE discussion for developmental cardiac effects to reflect the critical deficiencies in the Johnson et al. (2003) study. • EPA should also further clarify why the WOE does not support use of this endpoint to provide the representative POD for risk characterization especially at low environmental concentrations relevant to the POD and the low (ppb) air concentration that EPA derived from the Johnson et al. (2003) study. EPA should reconsider its assessment of the WOE for the developmental toxicity endpoint and whether it is appropriate to rely on a single study that is inconsistent with other studies when making its conclusions on developmental hazard.	EPA has modified the Risk Evaluation to more consistently emphasize the key immune endpoints. Additionally, much of the discussion on cardiac defects has been moved to Appendix F. The weight of evidence conclusions for the cardiac defects endpoint have not changed, but EPA has bolstered its support of selecting the two immune studies as the basis for risk conclusions.
51, 68	**PUBLIC COMMENTS:** In the WOE evaluation, EPA concludes that human studies, as a group, provide suggestive evidence for an effect of TCE on cardiac defects in humans; this is not an accurate reflection of the uncertainty and poor reliability of this evidence stream, which severely compromise data interpretation and integration resulting from the well-published high risk of bias associated with exposure characterization and confounding factors, as well as inconsistent results. • Considered in the context of largely weak study designs (cross-sectional and ecological), this evidence stream has been deemed inadequate for informing the TCE-fetal cardiac defect hypothesis and does not agree with prior TCE assessments. Earlier EPA assessments concluded that "overall, these epidemiologic studies are not sufficient to establish a causal link between TCE exposure and	EPA has accounted for these considerations in the assessment of study reliability. In most cases uncertainties surrounding exposure characterization are either applicable to both controls and treatment groups, or they lead to an underestimation of exposure. EPA agrees that these studies alone are not sufficient for establishing a causal link, however they do establish an association between TCE exposure and increased incidence of cardiac defects.

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	cardiac defects in humans." Wikoff et al. (2018) applied NTP's OHAT risk-of-bias framework to the TCE-fetal cardiac defect human studies, which focused on the "internal validity" of the study design and reporting and determined that the human TCE-fetal cardiac defect data were of insufficient quality to inform the direction of an effect. Wikoff et al. (2018) found no consistent evidence of fetal cardiac effects when integrating animal and epidemiological evidence.	
51, 60	**PUBLIC COMMENTS:** EPA inappropriately excluded two inhalation studies (Hardin et al., 1981; Healy et al., 1982). • Hardin et al. (1981) was scored "unacceptable" for Metrics 7 and 2; however, EPA had all of the study details in the underlying laboratory report (Beliles et al., 1980), which it scored overall high quality but failed to include in the WOE evaluation. • Healy et al. (1982) was scored "unacceptable" on Metric 12. It is clear investigators used a whole body, dynamic, single animal exposure cage for each test animal, which meets the definition of a "medium quality" for this metric.	(Beliles et al., 1980) was not included because the study report did not contain an indication that cardiac effects were specifically examined (See Appendix F.3.1). (Hardin et al., 1981) had several flaws, including an absence of details on TCE source, storage, and administration. Healy et al., 1982 scored unacceptable due to an absence of details on inhalation chamber and exposure method. This information was not provided in the study text.
51	**PUBLIC COMMENTS:** Due to the inaccurate absence of Beliles et al. (1980)/Hardin et al. (1981), and Healy et al. (1982) from the draft WOE, the current WOE conclusions are in error. Ultimately, EPA excluded inhalation studies from its WOE that would have demonstrated that the animal TCE-fetal cardiac defect data are strongly negative for the most relevant route of exposure for the exposure scenarios assessed.	
51	**PUBLIC COMMENTS:** EPA scored the TSCA Outcome Assessment Metric (#16) as "High Quality" for all five of the TCA/DCA studies, including the three earliest studies (Smith et al., 1989, 1992; Epstein et al., 1992); however, none of the studies observed atrial septal defects following high-dose exposure. This metric should have been scored "Low Quality" for failure to observe atrial septal defects. EPA did not score Metric #19, which	The majority of data quality criteria metrics apply to the overall study of interest and are independent of any particular endpoint target unless otherwise indicated by the study design. Occasionally a study will be split and evaluated for different outcomes, however all but a few

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	should be a scoring requirement for any study with teratogenic determinations. Study quality scores are inflated and reflect inconsistent application of scoring methods.	metrics are likely to be the same. All studies were reviewed by two subject matter experts with experience reviewing dozens of studies to ensure consistency in application of data quality evaluation across studies. EPA stands by its data quality evaluation of all studies.
51, 68	**PUBLIC COMMENTS:** EPA failed to separately score experiments reported in studies testing multiple animal species, minimizing negative TCE-fetal cardiac defect findings for most relevant exposure route (inhalation). This inappropriately reduced the impact of two separate developmental toxicity studies (Schwetz et al., 1975; Hardin et al., 1981) – each testing multiple mammalian species, on the TCE-fetal cardiac defect WOE.	
94	**PUBLIC COMMENTS:** Narotsky *et al.* (1995) is a flawed study that should have been excluded from the systematic review for methodological concerns. • The highest dose likely exceeded the metabolic saturation of TCE. Use of data at supra-saturating doses is problematic because there may be secondary high-dose specific effects that do not occur at lower doses where the toxicokinetics are linear. At oral doses below metabolic saturation where the data can be used quantitatively to extrapolate to realistic human exposures, the Narotsky et al. (1995) study found no adverse developmental effects.	
51	**PUBLIC COMMENTS:** After correcting several study quality scoring issues, and accounting for all of the relevant TCE-fetal cardiac defect animal experimental studies appropriately, an updated WOE is strongly negative.	
108	**PUBLIC COMMENTS:** EPA should also include/consider the following studies supporting a mechanistic linkage between TCE and developmental cardiac malformations prior to finalizing the risk evaluation: • Caldwell, Patricia T., et al. "Gene expression profiling in the fetal cardiac tissue after folate and low-dose trichloroethylene exposure." Birth Defects Research Part A: Clinical and Molecular Teratology 88.2 (2010): 111-127. • Selmin O.I., Makwana O., Runyan R.B. (2014) Environmental	The referenced Caldwell study is a follow-up to (Caldwell et al., 2008), which was included in the WOE analysis. This study examines gene expression changes following TCE exposure but does not provide any relevant novel information that would influence the WOE beyond what was already discussed from (Caldwell et al., 2008) and (Collier et al., 2003). (Selmin et al., 2008) is

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	sensitivity to trichloroethylene (TCE) in the developing heart. In: Gilbert K., Blossom S. (eds) Trichloroethylene: toxicity and health risks. molecular and integrative toxicology. • Jin, Hongmei, et al. "AHR-mediated oxidative stress contributes to the cardiac developmental toxicity of trichloroethylene in zebrafish embryos." Journal of hazardous materials 385 (2020) • Chen, Sheri, et al. "HNF4a transcription is a target of trichloroethylene toxicity in the embryonic mouse heart." Environmental Science: Processes & Impacts (2020).	a review paper that does not contain novel data. The 2020 studies were published well after the systematic review literature deadline and were not included in the WOE analysis, however they also do not contain novel information that was not already addressed by other studies that were included in the WOE analysis. EPA has added a list of studies in Appendix F.3.1 that were excluded during screening based on no direct assessment of cardiovascular outcomes.
51	**PUBLIC COMMENTS:** Several mechanistic studies and a few animal studies relevant to the TCE-fetal cardiac defect database are absent from the draft risk evaluation's TCE-fetal cardiac defect WOE. This is evidence of a flawed systematic review protocol, an inadequate integration of the database, and thus an incomplete risk evaluation.	
51	**PUBLIC COMMENTS:** EPA ignored the Caldwell et al. (2010) mouse transcriptomics study, not including it at all in the draft risk evaluation. This study failed to find any developmental toxicity in mice.	
51	**PUBLIC COMMENTS:** EPA ignored the *in vivo* arm of the Palbykin et al. (2011) study and instead scored the study based on the cell culture data.	(Palbykin et al., 2011) was not rated because there is not a direct connection of Sera2 gene expression to cardiac toxicity, however it was cited in Appendix F.3.3 as relevant to the non-monotonic dose response of the cardiac defects data. These findings were consistent both in *ex vivo* and cell culture.
51	**PUBLIC COMMENTS:** EPA's human evidence base is missing an occupational study by Tola et al. (1980), undermining the completeness of their human assessment. While this was another study of limited quality, it too failed to demonstrate an association between in utero TCE exposures and fetal cardiac defects.	This study was not cited in any previous WOE assessment, which were the basis of EPA's literature database for the WOE analysis.
51	**PUBLIC COMMENTS:**	

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	EPA excluded the ATSDR Camp Lejeune Study by Ruckart et al. (2013) from the TCE-fetal cardiac defect WOE because no formal analysis was conducted by the authors for the fetal cardiac defect endpoint, yet the fact that this exposed population had lower-than-background fetal cardiac defects should be included in the WOE.	The study authors were unable to perform any quantitative analysis and therefore conclusions cannot be made about cardiac endpoints based on this study.
67	**PUBLIC COMMENTS:** EPA seems to have missed the following relevant study: Trichloroethylene perturbs HNF4a expression and activity in the developing chick heart. Harris AP, Ismail KA, Nunez M, Martopullo I, Lencinas A, Selmin OI, Runyan RB. Toxicol Lett. 2018 Mar 15;285:113-120. doi: 10.1016/j.toxlet.2017.12.027.)	This study is included in the WOE analysis.
51	**PUBLIC COMMENTS:** It is unclear why EPA includes the rat intra-uterine pump exposure experiment described by Dawson et al. (1990), considering it "positive" TCE-fetal cardiac defect WOE. The irrelevant exposure route should have led EPA to disqualify this study from the WOE.	It is relevant for the plausibility of exposure leading to fetal cardiac effects.
51, 68	**PUBLIC COMMENTS:** EPA reviewed and scored two TCE-fetal cardiac defect positive studies as separate, single studies in their study quality assessment and WOE evaluation: Dawson et al. (1993) and Johnson et al. (2003). This decision artificially inflates the positive animal evidence in EPA's WOE evaluation because these publications represent the same animal study. EPA then considers them a single study for the dose-response evaluation. The recent risk of bias assessment by Wikoff et al. (2018) treated these studies as a single experimental study.	EPA stands by the results of the WOE analysis. In considering the conflicting evidence and varied opinions concerning the validity and relevance of the cardiac heart defects (CHD) database, EPA has added text throughout the RE (Appendix F.1, Section 3.2.4.1.6, Section 3.2.5.3.1, Section 3.2.5.1.6, and Section 3.2.6.1) acknowledging the uncertainties associated with this endpoint. EPA acknowledges that while there is qualitative support for the endpoint, based on uncertainties in the dose-response for this endpoint and other considerations EPA has selected immune endpoints as the best overall endpoints for risk conclusions (Sections 3.2.5.4.1, 3.2.6.1.1). However, various biological factors may lead to increased
99	**PUBLIC COMMENTS:** The Makris et al. review determined that, "despite the recognized uncertainties and limitations in the TCE database, the evidence supports a conclusion that TCE has the potential to cause cardiac defects in humans when exposure occurs at sufficient doses during a sensitive period of fetal development." This conclusion is warranted by the data that demonstrate or suggest a potential hazard to cardiac development, including epidemiological studies, developmental toxicology studies in	

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	rodents with TCE and its metabolites (DCA and TCA), avian *in ovo* studies, *in vitro* assays, and mechanistic data that form the basis of a preliminary conceptual model of an AOP for valvulo-septal defects resulting from TCE exposures.	susceptibility to CHDs, (*e.g.,* maternal age). Therefore, CHDs are now classified as a PESS consideration and the associated POD and risk estimates are included in the RE in consideration of PESS subset for which it is most applicable (*e.g.,* older mothers). Based on the inconsistent results for this outcome, EPA chose more consistently supported immune endpoints as the basis for risk conclusions.
78	**PUBLIC COMMENTS:** Multiple lines of scientific evidence clearly indicate that TCE increases the risk of fetal heart malformations. While the Johnson (2003) study plays an important role as the source of the POD for the fetal heart malformation endpoint for TCE, it is important to note that there are multiple lines of evidence that TCE and/or its metabolites increase risk of fetal heart malformation. These include: • studies *in vitro* and in multiple animal species that demonstrate a mechanism by which TCE and its metabolites cause fetal heart defects, • epidemiological studies suggesting TCE causes fetal heart defects in humans, and • *in vivo* animal studies that show a quantitative dose-response relationship between *in utero* TCE exposure and fetal heart defects. The body of science supporting the fetal heart malformation endpoint is substantial, as EPA acknowledged in its own draft risk evaluation.	
108, 99, 64	**PUBLIC COMMENTS:** Multiple lines of evidence support the finding that fetal cardiac malformations result from gestational exposure to TCE, including epidemiological evidence, laboratory animal studies, metabolism studies, and mechanistic studies which were indicated in the 2011 EPA IRIS TCE assessment and the 2016 review by Makris et al. (2017) • Support for TCE-induced fetal cardiac malformations based on WOE considerations has also been provided by the EPA Science Advisory Board (SAB) in its review of the IRIS TCE toxicological review; an EPA TCE Developmental Cardiac Toxicity Assessment Update ("Update") following the publication of the IRIS toxicological review; EPA's 2014 Workplan risk assessment, and EPA's response for a Request for Correction submitted by the HSIA regarding raising	

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	concerns regarding EPA's reliance on Johnson (2003). In Chapter 3 of the draft, EPA named developmental toxicity as among the most sensitive acute health effects associated with TCE exposure. However, in its risk determination, inconsistent with previous assessments and with summary statements in the body of the text, EPA states that the evidence contains uncertainties that decrease confidence in the endpoint of fetal cardiac defects. The rationale is unclear.	
99	**PUBLIC COMMENTS:** Even with the changes allegedly demanded by the Inter-Agency reviewers, the TCE draft risk evaluation presents a strong case for the sufficiency of the evidence of TCE-related cardiac effects. • It was concluded that "Overall, the database is both reliable and relevant and provides positive overall evidence that TCE may produce cardiac defects in humans based on positive evidence from epidemiology studies, mixed evidence from animal studies, and stronger positive evidence from mechanistic studies." As EPA indicated, "the fetal cardiac defects reported in (Dawson et al., 1993) and (Johnson et al., 2003) were identified as the most sensitive endpoint within the developmental toxicity domain and across all of the health effects domains evaluated in the TCE IRIS assessment."	
103	**PUBLIC COMMENTS:** EPA should utilize an established framework to organize evidence for MOA and to support decisions based on a side-by-side WOE comparison of alternative plausible MOAs. Examples: • AOPs to organize potential mechanisms into models that describe how exposure might cause cancer (*e.g.,* using the approach of the OECD AOP methodology). • The MOA approach initially championed by the World Health Organization (WHO)/International Programme on Chemical Safety (IPCS), which is utilized by other EPA program offices. • MOA confidence scores, as described by Becker et al. (2017).	The available mechanistic data on TCE supports multiple potential mechanisms that may contribute to developmental cardiac defects. However, there is not enough evidence for the majority of these to support development of a detailed AOP. EPA discusses mode of action considerations and the relevance to the observed non-monotonic dose response in Appendix F.3.3
94	**PUBLIC COMMENTS:** A systematic approach, such as the procedure developed by Becker et al.	

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	(2017), which enables side-by side comparison of numerical WOE confidence scores for different hypothesized MOAs, would provide the kind of scientific rigor in the selection of dose-response models that the amended TSCA requires in assessing potential cancer risk of TCE.	
51	**PUBLIC COMMENTS:** The putative AOP proposed by Makris et al. (2016) is incomplete (lacks empirical data for a molecular initiating event or subsequent early Key Events), but it provides a helpful approach to organizing the studies and their findings, as well as integrating in the higher level toxicological experiments (*in vivo*) and epidemiology data.	
108	**PUBLIC COMMENTS:** There is support for EPA's conclusion that "evidence of a single dominant MOA is not required in order for the data to support a plausible mechanism of TCE-induced congenital heart defects," particularly given that "teratogens may function through a multitude of pathways, often resulting in a constellation of effects." • While defined MOAs are not required for hazard identification, it should be noted that Makris et al. developed a preliminary AOP providing biological support for TCE-induced cardiac effects, specifically valvulo-septal defects, following developmental exposure. The WOE for congenital heart defects is robust, with corroborating data across mechanistic, animal, and human studies. A requirement that a MOA must be defined to legitimize this evidence is both unscientific and unprotective of public health.	
108	**PUBLIC COMMENTS:** EPA appropriately recognizes that developmental studies are relevant for evaluating acute exposure scenarios.	EPA acknowledges this comment.
66	**PUBLIC COMMENTS:** One of the criteria associated with a systematic review is a Risk of Bias. An element of that criteria is the source of study support. Except for Fisher et al. (2001), the entire body of literature challenging the link between TCE and heart defects (including Urban et al.) has been	EPA considered all data equally in evaluating the cardiac toxicity WOE.

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	supported by the HSIA and ACC industry associations. One could view the entire "controversy" on this link as a construct of these two organizations.	
Immunotoxicity evaluation		
SACC	**SACC COMMENTS:** One Committee member concluded that the TSCA program is struggling to integrate immunotoxicity into its chemical risk evaluations, as evidenced by the poor discussion and justification applied to inclusion/exclusion criteria used to identify key immunotoxicity studies and by the imprecision of terms used to discuss immunotoxicity in this draft risk evaluation.	EPA has improved the discussion of immunotoxicity in the assessment. Data on immune enhancement has been separated from discussion of immunosuppression, and additional studies have been added to the immunotoxicity hazard identification section (3.2.3.1.4). There is strong evidence in support of both autoimmunity and immune suppression as indicated throughout the Risk Evaluation.
SACC	**SACC COMMENTS:** Recommendation: Use and define more precise terms in discussing immunotoxicity. The draft risk evaluation uses imprecise language to discuss immunotoxicity. For example, the use of terms such as "allergic respiratory sensitization" and "sensitization/hypersensitivity" need to be better defined. Although such vague terms are often found in the literature, they can and should be replaced by more precise and informative terms (*e.g.,* one Committee member suggested using more precise designations such as Type I, II, III, or IV hypersensitivity).	
SACC	**SACC COMMENTS:** Recommendation: Clarifications and corrections are needed. Section 3.2.3.1.4, pp. 212-214; lines 837-895: In the overview of immunotoxicity and sensitization, there appears to be confusion regarding immuno-suppression vs. immuno-stimulation. The statements in lines 839-840 appear contradictory to the statement in line 868.	
SACC	**SACC COMMENTS:** Recommendation: Consider separating indicators of immune-enhancement and immunosuppression and discuss how these indicators reflect different MOAs. Based on the difference in mechanisms between acute and chronic immune effects, the draft risk evaluation should be especially careful not	

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	to suggest some false equivalence. The draft risk evaluation states that in general, immunotoxic effects in animals and humans were associated with an enhanced immune response rather than an immunosuppressive effect (draft risk evaluation, p. 212, lines 839-840). However, the first paragraph on animal data (draft risk evaluation, p. 213, lines 872-880) suggests that support for immunotoxicity is provided by decreased thymus weight and cellularity in mice (Keil et al., 2009). The Committee recommended that the risk evaluation not put indicators of immune-enhancement and immunosuppression in the same category and think more about MOA where these processes and indicators are different.	
103	**PUBLIC COMMENTS:** EPA should include a more complete discussion of the available literature on issues affecting immunotoxicity in the WOE section for this endpoint. Specifically, EPA should add additional explanation of the overall confidence in and uncertainties across the body of evidence, including additional discussion of: (1) the difference in risk profiles and etiology of autoimmune and immune effects, (2) alternative explanations that may be plausible for some or all of the observed associations, and (3) the strengths and weaknesses of the available literature. An enhanced WOE discussion would improve transparency in EPA's conclusions regarding hazard and its risk characterization.	
Choice of best representative POD		
SACC	**SACC COMMENTS:** Some Committee members commented that there is the impression of bias in the descriptions of the fetal cardiac malformations in relation to the literature, especially the Johnson et al. (2003) and the CRL (2019) studies. The Committee recommended that EPA consider a full and complete description of the issue (*i.e.,* why is this endpoint so controversial?) and provide a more complete discussion of other relevant studies to help explain the results relevant to data coherence between studies conducted by the same route of administration (*e.g.,* Is there coherence in the available literature? Is it consistent with oral, inhalation exposures or both?). Committee members brought up a concern related	EPA has expanded the justification for selection of the immune studies as the best overall endpoints. EPA believes these endpoints represent the "best available science" based on the weight of scientific evidence in accordance with TSCA and the use of these endpoints for risk conclusions was supported by SACC peer reviewers (https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0500-0111). TSCA requires to

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	to the questions raised publicly regarding alleged changes to the draft risk evaluation. The claim stated that the draft provided for interagency review identified fetal cardiac malformations as the most sensitive endpoint, and used this value to derive the PODs for making determinations of risk, a decision that was consistent with prior reviews of TCE (*e.g.*, EPA's 2011 IRIS review; U.S. EPA, 2011). This public allegation in part justified the Committee engaging in an extensive discussion of the draft risk evaluation's rationale for excluding fetal heart malformations as the endpoint for setting the POD.	select exposure and hazard values based on the best available science, not simply the lowest values. Additionally, EPA has expanded discussion of the history of (Johnson et al., 2003) and the cardiac defects endpoint in Appendix F.1. EPA routinely conducts Inter-Agency review of its TSCA Risk Evaluation before SACC peer review and public comments. Federal experts in toxicology, epidemiology, and industrial hygiene among other disciplines help EPA develop more comprehensive and rigorous risk evaluations. In this particular Inter-Agency review EPA discussed, among other things, the strengths and weaknesses associated with use of the cardiac defects endpoint as the basis of the risk conclusions. Based on these discussions, EPA concluded that whereas evidence indicates that CHDs may be of concern for susceptible subpopulations, the inconsistency of the data and reduced confidence in dose response results suggest that it is not the best indicator of TCE toxicity overall. For purposes of risk evaluations under TSCA, EPA chose to use immune endpoints as the indicator of TCE toxicity based on their consistency, reduced uncertainty, and robustness of the data. EPA has created a new subsection identifying and justifying the two immune endpoints as best overall for use in risk conclusions (Section 3.2.5.4.1).
100, 34	**PUBLIC COMMENTS:** EPA acknowledges an association between TCE and fetal cardiac malformations occurring at doses lower than those that cause any other adverse health effect. However, in a departure from prior EPA risk assessments, EPA fails to base its calculations of TCE's risk on that most sensitive endpoint. The draft should be revised to restore heart development as a driver of exposure standards.	
78	**PUBLIC COMMENTS:** EPA should use the fetal heart malformation endpoint as the critical endpoint for determining whether various uses of TCE present unreasonable risk. • OHA and DEQ disagree with the decision to not select fetal heart malformations as the critical endpoint because of the severity of the potential health outcome. EPA stated "Neither the statute nor the framework rule require that EPA choose the lowest [POD]." The lack of a requirement to use the most health protective POD does not preclude it, especially when good science indicates the potential for severe health outcome in a sensitive population. EPA should not use a less sensitive endpoint in lieu of a more sensitive endpoint just because the less sensitive endpoint has more scientific certainty. The available science justifies using the more sensitive fetal heart malformation endpoint as the POD for TCE.	
78	**PUBLIC COMMENTS:** OHA and DEQ have grave concerns that EPA has rejected the well-	

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	vetted, peer-reviewed science on fetal hemi malformations as the basis for making determinations about which types of product-use exposures (industrial, commercial, domestic, etc.) pose unreasonable risk in their TSCA draft risk evaluation. The POD for this health effect (endpoint) is important for the protection of a vulnerable population – developing human fetuses. The draft risk evaluation shows that nearly all types of TCE use would pose unreasonable risk to developing human fetuses, even with the most rigorous use of PPE. Ignoring this endpoint in making official risk determinations could allow continued, unsafe TCE exposures to developing fetuses if any future actions EPA takes to limit exposure do not consider the more sensitive endpoint of fetal cardiac malformations.	
73	**PUBLIC COMMENTS:** Study scoring is inappropriately used to support the use of immune-related endpoints rather than fetal cardiac malformations to derive PODs for determinations of risk.	
47	**PUBLIC COMMENTS:** We were struck by the tortured logic being applied to justify the choice of endpoints for the quantitative assessment of acute and chronic non-cancer effects, and then learned that Inter-Agency reviewers allegedly directed EPA not to use fetal heart defects, the most sensitive endpoint, for determination of unreasonable risk. We view this alleged intervention into the scientific assessment of a high-profile chemical as one of the most egregious acts we have witnessed in our collective century-plus years of experience at the agency. It raises the spectre that less-visible manipulations have occurred in earlier draft risk evaluations and prospects of the same for risk evaluations to come. The credibility of the once-promising amended TSCA risk evaluation program for existing chemicals is now shattered.	
47	**PUBLIC COMMENTS:** The PODs derived from the Johnson et al. study should be used in the assessment of all acute and chronic occupational exposure scenarios and all acute consumer exposure scenarios.	

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	• As currently articulated in the draft risk evaluation, it would appear that EPA is employing a new and unvetted policy of selecting the most "representative" over the most sensitive endpoint, an approach at odds with longstanding agency-wide risk assessment practices. The factors selected for consideration under this new policy do not include sensitivity and appear to be arbitrary and capricious, designed to provide EPA with complete discretion to ignore the most sensitive endpoint. • In addition to providing the most sensitive endpoint, congenital heart defects, the Johnson study has the lowest cumulative uncertainty factor and highest relevance to the endpoint of interest and human exposure scenarios of all the studies chosen for derivation of the POD. The low cumulative uncertainty factor is backed by the positive WOE supporting this study, with epidemiology and mechanistic studies compensating for the mixed evidence from animal studies. It is critically important that EPA not replace the protective public health policy of selecting the most sensitive endpoint with this arbitrary and capricious "representative policy." There is no scientific justification for this new policy.	
88, 86	**PUBLIC COMMENTS:** We are gravely concerned with EPA's failure to identify fetal heart defects, the most sensitive health outcome affecting the most sensitive group, as the key risk of exposure to TCE. This means that the chemical will not be regulated at a level to protect against this outcome. This lack of regulation grants a long-held wish of the chemical industry that ignores decades of scientific research.	
83, 36	**PUBLIC COMMENTS:** The studies are pretty clear that fetal cardiac defects occur at doses 500 times lower than the immune diseases that EPA is using for the maximum allowable exposure. Given that the best information we currently have strongly supports that TCE is toxic to human fetuses at much lower doses than EPA is considering for future regulations, then	

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	we MUST maintain the stricter regulations. It makes no humanitarian sense to use a 500 times higher maximum exposure dose until proven wrong.	
108	**PUBLIC COMMENTS:** EPA presents a rigorous case for the congenital heart defect endpoint throughout the draft, considering multiple lines of evidence that converge into an integrated strength area score of (+). EPA highlights the robust evidence base multiple times. This endpoint should be considered in the quantitative assessment of the health hazards of TCE.	
108	**PUBLIC COMMENTS:** EPA's reliance on immune-related endpoints, instead of congenital heart defects, for its determinations of acute and chronic risk deviates from scientific best practices, defies requirements under the law, and is not sufficiently protective of public health and vulnerable subpopulations. The WOE supports TCE-induced congenital heart defects. Multiple lines of evidence support the finding that congenital heart defects result from gestational exposure to TCE, including data from epidemiological, *in vivo*, and *in vitro* studies. This is the conclusion of the draft risk evaluation, as well as previous peer and SAB-reviewed analyses (*e.g.,* 2011 EPA IRIS, Makris et al., 2016). Failure to protect against the most sensitive endpoint, congenital heart defects, is a major concern.	
108	**PUBLIC COMMENTS:** The SACC meeting indicated that there was not a consensus among members over EPA's decision to jettison reliance on heart defects as the key driver for TCE's risks. • Some members believed this was a critical endpoint that was supported by the WOE, despite acknowledging that there was some uncertainty in the literature that posed challenges for moving from hazard identification to dose-response modeling. Other members also noted the extreme nature of scrutiny paid to studies identifying congenital heart defects in comparison to that applied to the immune studies, as well as the changes made in response to political interference.	

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	• Other members supported EPA's decision, arguing that the heart defect endpoint was an outlier, emphasizing flaws in supporting studies, and placing greater weight on studies sponsored by the chemical industry that did not replicate those effects. A question posed was: How can EPA protect against risks of a health endpoint that the WOE indicates is real and that some studies show occurs at very low doses, if there is a view by some that the data are not ideal for dose-response modeling? How would reliance instead on a non-developmental endpoint that shows effects only at higher doses fulfill EPA's responsibility under TSCA to identity and protect against risks to the most vulnerable subpopulation? EPA must rely on this endpoint to ensure protection a vulnerable subpopulation.	
106	**PUBLIC COMMENTS:** EPA's rationale for changing the representative acute non-cancer endpoint is unclear and inconsistent within the draft risk evaluation. • Throughout the draft, we found scientifically unsupported, unclear, and inconsistent statements around the evidence base for fetal cardiac defects and EPA's choice of representative acute non-cancer endpoint. • EPA's previous claims in its IRIS assessment and TSCA Work Plan, and current claims in Chapter 3 of the draft risk evaluation (Hazards), find that the fetal cardiac defects endpoint was the most sensitive (thus should be chosen as the representative non-cancer endpoint), with the support of animal, epidemiological, and mechanistic data. However, Chapter 5 of the draft risk evaluation (Risk Determination) rewrites the scientific evaluation of fetal cardiac defects, claiming that there are uncertainties that decrease EPA's confidence in this endpoint. This internal inconsistency and rewrite of the scientific evaluation suggests that there may have been some type of interference in this document. EPA chooses the immunosuppression endpoint proposed by Selgrade and Gilmour (2010), without justification for why the fetal cardiac defects endpoint was insufficient to serve as the representative endpoint	

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	and despite just stating that "confidence is *raised from the robust WOE analysis performed on the congenital heart defects endpoint.*"	
106	**PUBLIC COMMENTS:** EPA is inconsistent with its reporting of study conclusions throughout the draft risk evaluation. • For example, on p. 215, EPA states that Yauck et al. (2004) observed a strong relative risk estimate for cardiac malformations in infants born to TCE-exposed mothers aged 38 years or older, but later calls the Yauck conclusions equivocal or ambiguous, because the study "reported a positive association between congenital heart defects and TCE exposure only in older mothers, while younger mothers and the overall population had a null association," even though it is previously stated that "Maternal age is known to have a large influence on the incidence of congenital heart defects" and that "Among pregnant women, older women may be especially susceptible to TCE-induced cardiac defects in their offspring." These inconsistencies threaten the validity of the risk evaluation and appear to incorrectly downplay the strength of the fetal cardiac defect endpoint in support of an immunosuppression endpoint whose POD is orders of magnitude less protective.	The distinct statements are not mutually exclusive. There is statistically significant risk identified for older mothers, however there was a null association for mothers overall. Evidence such as the (Yauck et al., 2004) data supports the decision to consider the congenital heart defects endpoint only applicable to susceptible subpopulations.
106	**PUBLIC COMMENTS:** Chapter 3 of the draft risk evaluation is in conflict with respect to developmental endpoints. On p. 257, EPA states that "Confidence is reduced from a high due to the data quality scores, the wide range of PODs, and controversy over the most sensitive POD (Johnson et al., 2003). For developmental endpoints, there is some uncertainty extrapolating from chronic developmental toxicity studies to acute exposure, especially in assuming a consistent dose-response…Confidence is raised from the robust WOE analysis performed on the congenital heart defects endpoint (see Appendix G), the presence of a variety of endpoints including a study using acute TCE administration, and reduced uncertainty factors due to the use of PBPK model or allometric scaling." In the next line, EPA chooses the	EPA has added justification for the selection of the immune PODs as the representative acute and chronic endpoints and has highlighted their selection throughout the risk evaluation, including a new section, 3.2.5.4.1. The referenced values in IRIS (RfD, RfC) are based on multiple endpoints, namely the kidney toxicity endpoint and the autoimmunity endpoint in addition to fetal cardiac defects. Risk estimates for each of these endpoints are included in the risk evaluation, and the autoimmunity endpoint is the POD from (Keil et

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	immunosuppression endpoint proposed by Selgrade and Gilmour (2010) without providing justification for why the fetal cardiac defects endpoint was insufficient to serve as the representative endpoint. EPA asserts in the evaluation that the data for fetal cardiac defects is not robust enough to represent acute non-cancer endpoints and instead chooses immunosuppression as the sensitive endpoint for acute inhalation and dermal exposures as it is "…considered to be the most robust and best representative POD for acute non cancer scenarios." Although EPA indicates that the endpoint of fetal cardiac defects was not sufficiently robust and thus not a good candidate as the non-cancer endpoint for TCE, this is inconsistent with its IRIS assessment, which found that regarding fetal cardiac defects, "[t]here is high confidence in these noncancer reference values, as they are supported by moderate-to-high confidence estimates for multiple effects from multiple studies."	al., 2009), which was selected as the best overall chronic endpoint in this risk evaluation. Risk estimates for the cardiac defects endpoint are still included in the risk evaluation, however based on uncertainties in the dose-response for this endpoint and other considerations EPA has selected immune endpoints as the best overall endpoints for risk conclusions (Sections 3.2.5.4.1, 3.2.6.1.1). EPA does not directly compare numerical scores, just the overall bin. The metrics are not designed for that granularity. Additionally, 0.3 is a relatively large difference (almost no study scores higher than a 2 without being unacceptable, with higher scores indicating lower quality and 1.0 being the best possible score).
106	**PUBLIC COMMENTS:** EPA's choice of a representative acute non-cancer endpoint is less sensitive, less protective of vulnerable populations, nor consistent with best practices in scientific evaluation and use. • EPA indicated "…the POD for mortality due to immunosuppression from Selgrade and Gilmour (2010) is considered to be the most robust and best representative POD for acute non-cancer scenarios." However, it fails to sufficiently detail what makes this choice of endpoint more robust and the best representative. • This choice is in contrast to EPA's IRIS assessment, which derived its RfD for non-cancer effects of 0.0005 mg/kg/day based on the critical effect of heart malformations and concluded there was high confidence in this RfD. • The POD from the Johnson (2003) study is much lower than that from the Selgrade and Gilmour (2010) study, while data quality scores from both studies were similar (1.6 vs. 1.9). • EPA has failed to justify why it is unable to use the POD for fetal cardiac defects, which is orders of magnitude more protective than the immunosuppression endpoint, as the acute non-cancer endpoint.	

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	• If EPA were to pursue the representative endpoint of immunosuppression, EPA would be allowing acute exposures that are significantly greater than the POD for fetal cardiac defects and would fail to account for the particular sensitivity represented by developmental endpoints. • Choosing to use the immunosuppression endpoint in comparison to the fetal cardiac defect endpoint means discarding a more sensitive endpoint that has evidence of hazard to human health and which accounts for potential exposure to susceptible subpopulations, such as fetuses, pregnant women, infants, and children. Considering the disparities between PODs for the two endpoints and the potential human health ramifications due to this inadequately representative non-cancer endpoint for TCE, EPA should use fetal cardiac defects as the basis of the non-cancer acute health effects and the subsequent risk assessment.	
108	**PUBLIC COMMENTS:** During the SACC meeting, one reviewer noted several general population studies found associations between a variety of TCE exposure metrics and birth defects (central nervous system [CNS] and neural tube defects, congenital heart defects, oral clefts) and growth measures such as small for gestational age and term low birth weight. These studies involved numerous communities (Woburn, MA; Endicott, NY; northern NJ; Camp Lejeune, NC; Milwaukee, WI; and Tucson, AZ), state registry studies (MA, TX), and a national birth defects prevention study. Failing to include this endpoint in EPA's determination of unreasonable risk would ignore a documented and serious health concern that should play a major role in setting limits on TCE exposure and use.	The risk evaluation discusses these epidemiological studies and associated effects in Section 3.2.3.1.6. Risk estimates are provided for multiple developmental endpoints covering developmental neurotoxicity, developmental mortality, and congenital defects. EPA has the discretion to make unreasonable risk determinations based on other risk benchmarks or factors as appropriate. EPA's unreasonable risk determination (Section 5) considers multiple risk-based factors including the uncertainties in the analysis (Section 4.3). In considering uncertainties surrounding these endpoints (Section 3.2.6.1.1), the immune endpoints were determined to be the best overall endpoints for risk conclusions and risk determinations (Section 3.2.5.5.1).
105	**PUBLIC COMMENTS:** Developmental effects are not adequately considered in the draft risk evaluation. As a result, the evaluation does not sufficiently address the pregnant woman and her developing fetus, which represent a susceptible subpopulation. The draft risk evaluation presents evidence that TCE can cause developmental toxicity, cites studies that can be used for hazard	

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	identification and dose-response assessment, and concludes that the WOE indicates TCE produces fetal heart defects. Despite this finding, the risk determination (Section 5) does not consider this endpoint and does not provide an adequate rationale for dismissing developmental studies that were previously used in the peer-reviewed IRIS document (U.S. EPA, 2011). Developmental effects are often the most sensitive endpoint. EPA should develop and present toxicity values that are sufficiently protective against the adverse developmental effects of TCE.	
90	**PUBLIC COMMENTS:** In previous risk evaluations for TCE under TSCA, EPA has consistently concluded that the weight of the scientific evidence supports teratogenicity of TCE exposure and fetal heart malformations. Fetal heart malformation has been considered the standard for the most sensitive endpoint for TCE exposures, and consequently these adverse effects have driven risk determinations for acute and chronic TCE exposure. Since the last risk assessment for TCE, a WOE analysis of epidemiological, toxicological, *in vitro*, *in ovo*, and mechanistic/AOP data concluded that TCE has the potential to cause cardiac defects in humans when exposure occurs at sufficient doses during a sensitive window of fetal development (Makris, 2016). The study that had formed the earlier basis for this association by Johnson et al. was reaffirmed as suitable for hazard characterization. However, this draft risk evaluation downgrades consideration for these previously accepted studies by saying that there may be scientific uncertainties associated with TCE exposures. This is inconsistent with the weight of the scientific evidence as described by Makris et al. As a result of the downgrade of previously accepted scientific evidence, this draft risk assessment has chosen a much less vigorous endpoint that is based on immunotoxicity impacts. Exposure limits based on immune effects are far higher in this risk assessment than those for fetal heart malformation and would therefore inadequately protect developing fetuses. This risk evaluation dismisses the WOE supported by sound science with defective analysis, even when the most vulnerable of special populations, the developing fetus, is put at	EPA's WOE analysis is consistent with the conclusions of (Makris et al., 2016). (Makris et al., 2016) did acknowledge that the database and dose-response for the cardiac defects endpoint had significant uncertainty, however the weight of the scientific evidence supported the association between TCE exposure and developmental cardiac malformations. This risk evaluation comes to the same conclusion based on a rigorous, detailed WOE analysis that considers all relevant studies in the database scores for reliability, relevance, and strength of the response. EPA does not consider costs or other non-risk factors in the risk evaluation.

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	higher risk of fetal malformation. Clearly, EPA has replaced the Precautionary Principle with a Cost-Benefit Analysis calculation. We strongly urge EPA to revert to a weight-of-the-scientific-evidence approach for their risk assessment and prioritize vulnerable populations, in this case fetuses, in the final evaluation for TCE.	
99	**PUBLIC COMMENTS:** EPA is wrong that its "representative endpoint" of immune effects "would address other identified risks." The acute HEC99 (99th percentile for human equivalent concentration [HEC]) for immune system effects is 470 times higher than the acute HEC99 for heart malformations. This significant disparity translates into large differences in the acute MOEs for the two endpoints. For example, EPA calculated acute inhalation MOEs (high-end exposure/no PPE) for workers in batch open top vapor degreasing operations of 0.000014 for heart defects but 0.67 for immune effects. Both MOEs are far below the benchmark MOEs for these endpoints but the MOE for heart defects is over two orders of magnitude below the MOE for immune effects. Accordingly, the large number of pregnant women exposed to TCE would be unprotected from fetal heart defects in their offspring by an exposure limit based only on immunotoxicity.	EPA has clarified that these risk estimates would address "most" other identified risks. EPA has also added additional POD derivations for the key immune endpoints specific to occupational scenarios in order to account for increased exposure due to elevated breathing rates in workers. For these occupational PODs, the resulting chronic risk estimates based on (Keil et al., 2009) are within 2.6-fold of the results for Johnson et al., 2003 when accounting for differences in benchmark MOE. Additionally, EPA has increased confidence that the (Keil et al., 2009) MOEs are applicable to the entirety of the population evaluated in the risk evaluation.
99	**PUBLIC COMMENTS:** The claim that the data supporting immune effects are significantly more "certain" than the evidence of heart defects is incorrect and based on a selective and misleading comparison of the WOE for the two endpoints. According to EPA, "the POD for mortality due to immunosuppression is considered to be the most robust and best representative POD for acute non-cancer scenarios." • However, EPA's considerations for selecting this endpoint also apply to the heart defect database (*e.g.,* heart malformations are an extremely "severe" effect; the Johnson study used a "broad dose range;" the "dose response curve" in Johnson was clear and consistent; and while Johnson was a repeated-dose study, EPA's longstanding policy is that a single exposure to a chemical within a	EPA disagrees with the commenter that there is not increased confidence in the immune endpoints. While all studies selected for dose-response analysis are medium or high quality and contain broad dose ranges and sensitive endpoints when possible, they still contain varying uncertainties, resulting in varying confidence in the resulting POD. EPA agrees that data quality is only one aspect of consideration for selecting robust endpoints, however the immune endpoints involve significantly less uncertainty in the dose-

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	critical window of fetal development can cause adverse effects.) The different quality scores of the two studies, "medium" for Johnson and "high" for Selgrade and Gilmour, are unimportant compared to their strength in demonstrating adverse effects and the overall WOE supporting their findings. • UFs for immune effects were higher than for the fetal heart malformations. The UF for fetal heart defects was 10 and for acute immunosuppression effects was 30 "because the data was not subject to PBPK modeling and therefore a HEC99/HED99 value was not applied which would have accounted for human toxicokinetic variability." • EPA expressed concerns about the Selgrade study in its draft risk evaluation, observing that a "reliable BMDL could not be obtained from the percentage infected data because BMDs and BMDLs from all models were well below the lowest data point and cannot be considered reliable." The SACC should recommend that EPA revise the draft to use the heart defect data for addressing TCE's acute and chronic risks to human health and, as the most sensitive endpoint, the key driver for determining whether TCE presents an unreasonable risk of injury.	response results. Additionally, the (Selgrade and Gilmour, 2010) endpoint now also has a UF =10 because EPA has run the study data through the PBPK model to obtain more accurate dose-response results, further increasing confidence in the endpoint. The "percentage infected" data was not used for POD derivation, so those results have no impact on confidence in the POD for mortality. EPA presents reasoning for selection of the two immune endpoints as the best overall acute and chronic PODs in Section 3.2.5.4.1.
108	**PUBLIC COMMENTS:** It is inappropriate to use study quality as the sole basis for endpoint and study selection. Study quality is *an* appropriate consideration of the adequacy of published research to serve as the basis for dose-response analyses. After inappropriate studies are eliminated as candidates for dose-response analyses, other considerations, such as sensitivity, should form the basis for endpoint selection for dose-response analysis. • EPA erroneously prioritizes study quality above all else in selecting the immune endpoints as the basis for its risk determinations for acute and chronic non-cancer risks. • When selecting *between* studies of the same endpoint EPA reviews both High and Medium quality studies and chooses to advance the Medium quality studies to represent those endpoints.	

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	This approach seems intended to allow EPA to derive less-protective hazard values and use them to underestimate risk, to the benefit of industry, allied interests and to the detriment of public health.	
105	**PUBLIC COMMENTS:** "Medium quality" evidence should not be disregarded. If EPA limits its evaluations to consider "high quality" information only, then it will severely impair EPA's ability to develop health protective determinations or guidelines. For many chemicals, there is a limited amount of high-quality toxicological information available.	
74	**PUBLIC COMMENTS:** EPA's numerical scoring plays a nefarious role in this draft, whereby EPA claims the evidence for fetal cardiac defects are of "medium" quality while that for immune effects is "high" quality leading EPA to rely on risk estimates orders of magnitude less than should be the case.	
Selgrade and Gilmore (2010) as source of best representative POD for acute effects		
SACC	**SACC COMMENTS:** Recommendation: Highlight the uncertainty inherent in relying on one study to establish the immune endpoint. • The Selgrade and Gilmour (2010) study represents an appropriate choice for evaluating the acute effects of TCE on the immune system, although it has not been validated. • The draft risk evaluation must make clear that acute immuno-suppressive response is based on a single study. It should be acknowledged that while this study is novel with respect to TCE, it by no means reports a novel response or study design in the inhalation toxicology literature. The text should highlight the higher uncertainty inherent in relying upon a single study in isolation to evaluate the most sensitive response.	(Selgrade and Gilmour, 2010) is actually a repeat of (Aranyi et al. 1986), which identified a lower NOAEL but had issues with mortality in controls. Therefore, it was not a completely novel study or result and the finding is not only based on a single study. Additionally, the 25 ppm NOEL is in the same range as the lowest observable effect for the vacuolation of Clara cells reported after a single 6-h exposure to TCE concentrations as low as 20 ppm in CD-1 mice (Odum et al., 1992).
SACC	**SACC COMMENTS:** While six valid criteria were listed in justification of utilizing the Selgrade and Gilmour data, none of these points really address whether this endpoint is the most representative or most sensitive and, therefore, the most protective. This conclusion should be more directly stated.	The selection of the immune endpoints as the best overall endpoints for risk conclusions has been made more clear throughout the document and is established in a new Section 3.2.5.4.1.

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SACC	**SACC COMMENTS:** The draft risk evaluation should consider reducing the POD based on the extrapolation of a reasonable sublethal effect. While the use of mortality as an endpoint is both clinically relevant and unequivocal, it brings into question whether this is effective as a protective POD, because one would expect other functional effects that precede mortality to occur at even lower doses.	EPA accounts for the severity of the endpoint by using a 1% BMR. EPA was unable to BMD model sublethal endpoints from the study, however any sublethal effects would be subject to a higher BMR which would be less sensitive than the 1% BMR that was used. Selection of a lower BMR based on the severity of an effect (referred to in the Guidance as a "frank effect") is consistent with EPA BMD guidance (U.S. EPA, 2012a). Considerations for BMD modeling are provided in Appendix G. The committee appears to have confused the data for number of mice infected with the data for mortality. EPA ran BMD modeling for both endpoints. Table_Apx F-5 (now labeled Figure_Apx F-5) is the plot for number of mice infected, which was not considered reliable. The data for mortality was instead used for dose-response analysis and POD derivation. EPA agrees the use of mortality may underestimate risk, however the use of a sublethal endpoint would also involve a higher BMR selection. EPA will acknowledge this in the uncertainties section. EPA modeled the number of mice infected as an attempt to examine sublethal effects, however sample sizes and dose selection for that and other sublethal endpoints were insufficient for use in dose-response.
108	**PUBLIC COMMENTS:** A POD based on mortality from the Selgrade and Gilmour study is not protective of public health. • SACC panelists highlighted that using mortality to derive the POD results is an underestimation of sublethal effects. There are expected to be toxic effects on the immune system below the level that causes death. As such, this mortality endpoint is not expected to be sufficiently protective against more sensitive, sublethal endpoints across the population. EPA guidance directs EPA to choose the most sensitive endpoint, which is congenital heart defects in the case of TCE.	
SACC	**SACC COMMENTS:** • Selection of a 1% benchmark response [BMR] due to lethality is consistent with other POD derivation in the document (*e.g.,* congenital heart defects), but it is not clear whether this is consistent with EPA policy or is fully a professional judgment call by the authors. For the sake of transparency, this should be explained. • The benchmark MOE based on UFs is clearly described; however, a more detailed description would be preferable relative to the choice of UF_A and UF_H based on the fact that such a conservative POD (based on 1% BMR) is selected. • To several of the Committee, the fit of the data is unclear in the Benchmark Dose Software (BMDS) Figure (Appendix F, p. 599, Table-Apx F-5) and the model fit is questionable. The data from Selgrade and Gilmour (2010; *i.e.,* the doses presented) do not match up with those described in the text (*i.e.,* 0, 80, 100, 200 ppm	

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	presented; 0, 5, 10, 25, 50, 100, 200 ppm, but not found in BMDS model); moreover, measures of variance are not provided in the paper. • The data used to generate I-bars in the BMDS model were not clear to some of the Committee. Some on the Committee recommended not trying to fit those data, instead, but suggested using the no-observed-effect level (NOEL) of 100 ppm as a POD instead.	
95, 103	**PUBLIC COMMENTS:** There is some question as to whether the immunosuppression in mice observed by Selgrade and Gilmour is relevant to assessing acute risks to human. Mice exhibit a specific lung toxicity to chemical agents like TCE that may contribute to the observed inflammatory response and resulting mortality. The response reported could be associated with effects on Clara cells which are enriched in mice relative to rats and humans and could make mice uniquely vulnerable to infection. Without confirmation of a similar response in rats, it is not clear what role mouse lung-specific toxicity plays in the increased mortality seen in the TCE-exposed mice. It should be considered whether the dose in this study was of a level that could cause respiratory irritation.	The observations and dose-response observed in Selgrade and Gilmour, 2010 are consistent with those observed in chronic immunosuppression studies (Sanders et al., 1982; Woolhiser et al., 2006) on both mice and rats.
105	**PUBLIC COMMENTS:** The assessment of acute exposures should be based on developmental toxicity. • Although the draft describes how developmental endpoints are relevant to acute scenarios, consistent with EPA guidelines, a different endpoint was ultimately chosen (mortality due to immunosuppression) because "there is some uncertainty extrapolating from chronic developmental toxicity studies to acute exposure, especially in assuming a consistent dose-response…this may possibly result in an overestimation of risk for some scenarios." • EPA should include developmental toxicity in the assessment of acute exposures, since this approach would be health protective and follow EPA guidance. More specifically, EPA should use the POD from Kiel et al. (2009), with a total UF of 100, for assessment of	Multiple developmental endpoints are included in risk estimation of acute exposures. MOEs are provided for congenital heart defects, developmental neurotoxicity, and developmental mortality. EPA would not consider applying a chronic POD to an acute scenario when there is a robust study evaluating acute exposure. The (Keil et al., 2009) is not comparable to the (Selgrade and Gilmour, 2010) study, as they evaluated differing exposure scenarios and observed different immune outcomes.

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	acute exposure scenarios, rather than the endpoint of mortality due to immunosuppression (Selgrade and Gilmour, 2010). This should be done to provide better protection of developmental toxicity.	
Keil et al. (2009) as source of best representative POD for chronic effects		
SACC	**SACC COMMENTS:** Recommendation: Reevaluate the quality ratings of the four chronic immunotoxicity studies by Keil et al. (2009), Kaneko et al. (2000), Sanders et al. (1982), and Woolhiser et al. (2006). These studies have significant limitations that should affect their quality rating (all currently medium or high). • Considerations relevant for evaluating immunotoxicity studies include: (1) whether the choice of animal model and methodology are optimal for the scientific question being asked, (2) whether the proper controls were used, such that the reader can determine whether the immune assay actually worked, and (3) whether the data are properly evaluated and the conclusions reached were legitimate. These criteria need to be incorporated into the study rating. • It is not clear how the Keil et al. (2009) study was assigned a "high" quality rating when critical information regarding exposure is not provided (*e.g.,* neither purity, stability, nor homogeneity of TCE concentration is reported; although water concentrations (actual dose applied) were analyzed, those data are not provided (only nominal dose levels reported)) and calibration of the biomarker is not discussed. Dose levels are misreported in the draft risk evaluation. • Sanders et al. (1982) offers only very brief descriptions of methodology and statistics that are supposedly required for an adequate rating. The study used a variety of assays to examine multiple immune parameters. However, only some of the results were consistent, and/or associated with adequate controls. Overall, it is difficult to pick a consistent targeted effect on the immune system from the Sanders et al. (1982) study. • It is not clear why Woolhiser et al. (2006), which only showed an effect at one concentration of TCE, should be chosen as a key study.	These factors were already all accounted for in the data quality evaluation. Details are provided in supplemental files. A study does not need to score a high in every individual metric in order to be scored a High overall. The dose levels are correct in the Risk Evaluation. It appears that the dose levels are incorrectly presented in the abstract of the study, which may have caused the confusion. Data quality is not necessarily influenced by the results, only how well the study was performed and reported. However, this inconsistent response among results is further justification for not choosing (Sanders et al., 1982) as the representative study for the immune domain. (Woolhiser et al., 2006) was not selected as the representative study for immunosuppression ((Sanders et al., 1982) was), but the Woolhiser study is the only immune study that identifies a NOAEL. This is a benefit of the study and not a negative. (Kaneko et al., 2000) was not selected as the best study for autoimmunity ((Keil et al., 2009) was), so these considerations were taken into account.

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	The results were re-reported by Boverhof et al. (2013), which should not be considered a separate evaluation of immunosuppression. • The Kaneko et al. (2000) study, apparently chosen as a key study to illustrate how chronic TCE exposure causes immunotoxicity in an autoimmune-prone mouse model, reports on pneumatosis cystoides intestinalis, which is not, however, an autoimmune disease. In addition, MRL lpr/lpr mice are not a good model to examine chemically induced autoimmunity. It is not clear why this paper was selected over several other papers using superior animal models that have examined how chronic TCE exposure impacts autoimmune disease (*e.g.,* Griffin et al., 2000; Gilbert et al., 2009; and Wang et al., 2012).	
SACC	**SACC COMMENTS:** Recommendation: Add and discuss autoimmunity studies performed in different rodent models and with humans. • The Keil et al. (2009) paper is useful for evaluating the effects of chronic TCE exposure on the development of autoimmune disease in non-autoimmune-prone mice. However, the draft risk evaluation should also include at least one study that examined the effects of chronic TCE exposure on disease progression in autoimmune-prone mice. Because such mice can represent the human population most susceptible to the autoimmune-promoting effects of TCE, this inclusion is important. There are several studies that use models other than the NZBWF1 mice used in the Keil et al. (2009) study, including Griffin et al. (2000), Gilbert et al. (2009), and Wang et al. (2012). • HECs from other studies are markedly different from these calculated from the Keil et al. (2009) study. How does EPA explain the large differences in HECs compared with other data investigating the immunological endpoint? The Committee suggested that EPA consider as high-quality inhalation studies only those that provide analytical chemistry results confirming exposure. • The autoimmune response study in rodents is supported by data in	All recommended studies in this comment have been added to the immunotoxicity Hazard ID Section, 3.2.3.1.4. The key study of Kaneko et al, 2000 was already included, which evaluates autoimmune-prone mice (although previous comments indicate it may not be the best model). The POD from (Keil et al., 2009) is consistent with the POD from the developmental immunotoxicity study (Peden-Adams et al., 2006). Additionally, almost all other studies including the other autoimmunity study were LOAELs, so it cannot be determined that they had a higher NOAEL. The other autoimmunity study, (Kaneko et al., 2000), was also of much shorter duration so a higher POD is expected. Finally, (Keil et al., 2009) represents a sensitive clinical marker (hence the smaller UF_L) and would therefore be expected to be observed at a

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	humans suggesting there are potential immune hypersensitivity responses to TCE. Suggested human studies include: Bond (1996), Chittasobhaktra et al. (1997), Nakajima et al. (2003), Xu et al. (2009), Liu (2009), and Kang et al. (2018).	lower dose than the more severe effects observed in other studies.
SACC	**SACC COMMENTS:** Recommendation: Provide the scientific rationale for selecting the Keil et al. (2009) study for evaluating chronic non-cancer effects given its deficiencies. Several members of the Committee voiced concerns over the use of Kiel et al. (2009) study. • Doses used are outside the range used in other immunotoxicity studies. • One Committee member commented that the data are of questionable significance because there seems to be a lack of dose response. • Normal humans are not well represented by a genetically-prone strain, the data were generated from another pathway of exposure (oral) than is considered in the human COU, and only nominal concentrations were reported. • In Table 3-14, no explanation for the selection anti-ds and ssDNA antibodies as endpoints is given, and the levels of anti-dsDNA antibodies at 14,000 ppb in both normal and genetically prone mice are nearly identical to controls at 36 weeks. Qualification of this biomarker, along with a lack of justification, suggest that these data are not appropriate for use in this manner. • The draft risk evaluation suggests that TCE has both immuno-suppressive and autoimmunity properties. A biologically plausible explanation for how this might happen should be provided. • The authors also state that there is no statistically significant difference in thymic cellularity (p. 244, lines 2251-2257). This equivocal cellularity issue is a recurring problem. • The thymus mass effects measured may not be reliable, given the subjective nature of the assay, and because the thymus must be removed and trimmed, which unavoidably introduces technique related variability in weight determination. TCE-induced thymus	EPA provides justification for the selection of the best overall studies in Section 3.2.5.4.1. The POD from (Keil et al., 2009) was based on responses in normal mice, not autoimmune-prone mice. Increased autoantibodies were not observed in the autoimmune-prone strain (NZBWF1) tested in parallel .While there was not a consistent dose-response for autoantibodies (responses are similar or even decreased at the higher dose), this inconsistent dose response is in agreement with results from autoimmune-prone MRL +/+ mice in (Griffin et al. 2000). The non-standard dose-response was also considered in assignment of a UF_L of 3 instead of 10. EPA has updated the description of the POD to indicate that it is no longer based on thymic changes because those are insufficiently adverse or reliable. (Keil et al., 2009) was assigned $UF_L = 3$ (instead of 10). Detection of anti-nuclear antibodies (ANA) is a long-established clinical marker of autoimmune connective tissue diseases (*e.g.,* lupus). Specificity of ANA for autoimmune disease states can be low, however anti-dsDNA antibodies have been shown to be quite specific and are rarely detected at elevated levels in

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	weight changes were inconsistently observed between the two mouse strains. • For dsDNA and ssDNA, one Committee member noted that in all cases the high-dose groups exhibit a lower (average) response than the low dose groups, suggesting that the lowest-observed-adverse-effect level (LOAEL) should be the high-dose group, not the low-dose group. • Age-dependent differences in responses were observed in NZBWF1 mice, but not in B6C3F1 mice. It was not clear to some Committee members whether the inconsistent minimal effects observed in the B6C3F1 non-sensitive mouse have any clinical relevance. Other Committee members disagreed and pointed to multiple figures in the Keil et al. paper that show legitimate levels of toxicant-induced increases in antibodies. While dose responses are not very evident, TCE effects are evident.	healthy patients (Kavanaugh et al., 2000; Wichainun et al., 2013). Therefore, the results from (Keil et al., 2009) do represent an adequate biomarker of autoimmunity, and the selection of $UF_L = 3$ is justified due to the observed effect being considered an early, subclinical or pre-clinical early marker of disease and the non-standard dose-response observed in the study. SACC comments above (p. 249) indicate issues with the (Sanders et al., 1982) study, namely that only some of the results were consistent, and/or associated with adequate controls. Additionally, both are LOAELs, and (Keil et al., 2009) tested a lower dose range so was therefore more sensitive to effects at lower doses. Therefore, while both studies were selected for representing their respective chronic immune endpoints (immunosuppression for Sanders, autoimmunity for Keil), (Keil et al., 2009) was selected as the most robust and sensitive study for both the immune domain and overall chronic non-cancer endpoints.
SACC	**SACC COMMENTS:** Recommendation: Consider increasing the autoimmunity effect UF_L to account for uncertainties in the clinical significance of autoantibodies. • The Committee was comfortable with using a UF_L (LOAEL-to-no-observed-adverse-effect level [NOAEL] UF) of 3 for the Keil et al. (2009) study because the LOAEL is based on an early clinical marker (autoantibodies). Because anti-DNA autoantibodies are often the precursors for actual autoimmune disease, some Committee members suggested that a UF_L=10 should be assigned to their detection. Not all Committee members agreed with this increase, however, depending upon their confidence in the significance of this pre-clinical endpoint.	
95, 103, 94	**PUBLIC COMMENTS:** Concerns with using data from Keil et al. to drive a toxicity value. • A few SACC members discussed whether the antibody response reported by Keil et al. should be considered evidence of an adverse effect or only a biomarker. It was noted that the response was reported in the insensitive mouse strain but not in the strain with	

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	autoimmune sensitivity (*i.e.,* NZBWF1). • With limited histopathology evaluation (only the kidney), the autoantibody results lack confirmatory adverse response verification as to other organs and tissues that can be impacted. • The DNA autoantibody response reported by Keil et al. was erratic, noisy, and did show a non-dose response. • The draft risk evaluation should note that the effects observed by Keil et al. (2009) do not allow for derivation of a POD or reference concentration/dose. EPA should reconsider the Sanders et al. (1982) and Woolhiser et al. (2006) studies as more reliable critical studies for defining PODs and reference dose/concentration determinations. EPA should base its analysis of chronic, non-cancer risks on data from studies reporting immunosuppression rather than on the Keil et al. study.	
94	The serum DNA autoantibody responses reported in the study by Keil et al. (2009) is considered to be unreliable for derivation of a chronic non-cancer toxicity value. This study had: • Lack of analytical verification of dosing concentrations (the study indicated that analytical measurements were done by an outside laboratory, but the data were not provided); descriptions of measures taken to minimize volatility were also not provided. • Lack of biological plausibility with no accompanying pathological changes and the same effects not seen in autoimmune-prone mouse strain. • Lack of dose-response seen for most measurements at most time points throughout the study. • Inadequate number of dose groups for dose-response modeling. Additional studies are needed to substantiate the findings, with a clear link to "disease expression and pathology," before it can be considered sufficiently reliable to be used for risk assessment purposes.	
SACC	**SACC COMMENTS:** Recommendation: Consider using Sanders et al. (1982) to set the immunotoxicity POD.	

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	• Some Committee members suggested that EPA consider using an immunotoxicity study with a clearer dose-response for evaluating chronic non-cancer effects. One Committee member suggested using the study by Sanders et al. (1982) that resulted in suppression of humoral and cell-mediated immunity in female CD1 mice. Another Committee member disagreed, finding the Keil study superior to the Sanders study and hence noted that it is appropriate to use the Keil study in establishing the POD for immunotoxicity.	
94	**PUBLIC COMMENTS:** Other concerns with the Kiel et al. (2009) study: • Thymus weights are prone to inaccuracies; therefore, interpretation of the change observed is uncertain in the absence of any other clear treatment-related effects. • Lack of a water-only control group to rule out potential effects from the 1% emulphor. • Lack of information on whether 1% emulphor impacts TCE toxicokinetics (*e.g.,* absorption and distribution).	
94	**PUBLIC COMMENTS:** EPA's systematic review of Keil et al. (2009) reflects a naïve understanding of the technical difficulties with administrating TCE in drinking water in animal studies and is based on presumptions rather than analytical data; leading to an overestimation of the study quality. • The metrics for "Preparation and Storage of Test Substance" and "Consistency of Exposure Administration" were given "Medium" and "High" scores, respectively; and for both metrics, EPA concluded that "TCE levels were confirmed." Yet, there are no analytical data in the Keil et al. paper to support that conclusion. EPA relied on a statement saying that it was done. EPA gave a "High" score for "Exposure Route and Method" with the comment "Frequent changing of water with exposure level analysis to avoid decreased dosing to vaporization."	
94	**PUBLIC COMMENTS:** EPA is encouraged to consider endpoints from two other immunotoxicity	

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	studies given "High" data quality scores in the systematic review for the POD for chronic non-cancer exposures: Sanders et al. (1982) and Boverhof et al. (2013). Both studies reported treatment-related effects in conventional assays measuring immunosuppression in mice and rats, which is consistent with the effects on the immune system seen in acute TCE exposures by Selgrade and Gilmour (2010).	
108	**PUBLIC COMMENTS:** EPA has not provided sufficient justification for dismissing decreased thymus weight from the risk evaluation process. • Departing from the 2014 Work Plan Assessment, EPA did not consider decreased thymus weight and cellularity (observed in Keil et al., 2009) in the risk estimation process for immunotoxicity because it deemed these endpoints to be "insufficiently adverse compared to other endpoints." • The 2011 IRIS assessment considered this as a candidate critical effect.	
45	**PUBLIC COMMENTS:** The TCE safe chronic dose in EPA's IRIS database (a RfD) is based on the same key study as in this draft (Kiel et al). Yet the IRIS RfD is ~10 times lower (safer) than the current draft. EPA must explicitly justify what factors caused the change.	The cumulative UF for (Keil et al., 2009) in the IRIS assessment was higher based on a UF_L of 10. EPA evaluated consideration for the UF_L and determined that $UF_L = 3$ was most appropriate based on autoantibodies representing an early, subclinical effect. The TCE Risk Evaluation does not state a reference dose or concentration, so there is no RfD provided for making a direct comparison. (Keil et al., 2009) was assigned $UF_L = 3$ (instead of 10). Detection of anti-nuclear antibodies (ANA) is a long-established clinical marker of autoimmune connective tissue diseases (*e.g.,* lupus). Specificity of ANA for autoimmune disease states can be low, however anti-dsDNA
108, 105	**PUBLIC COMMENTS:** A UF of 10 instead of 3 should be used to convert from the LOAEL to a NOAEL for the autoimmunity endpoint (Kiel et al., 2009). This would provide better protection against developmental toxicity in the assessment of chronic exposures. • During the SACC meeting, several panelists criticized EPA's decision to use a value of "3", rather than the default of "10," UF_L for the Keil et al. autoimmunity endpoint. • EPA justified the decision to use a partial value of 3 rather than a full factor of 10 by stating that "the observed effect is considered an early, subclinical or pre-clinical early marker of disease." However, autoimmunity (*i.e.,* changes in antibody levels that impair the body's	

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	ability to fight viruses and other infections) should itself be considered a relevant immune effect rather than only a precursor or subclinical marker. This scenario could be viewed as analogous to considering liver enzyme changes as a marker of liver toxicity. • In deciding the appropriate UF, other severe effects of TCE should be considered, namely the evidence of developmental toxicity and the low concentrations at which developmental effects were observed. Since the endpoint from the Kiel et al. study is used as the critical endpoint for all non-cancer effects, the maximum UF_L of 10 should be used (bringing the total UF to 100 for the endpoint), to ensure that the threshold based on this study will protect against developmental toxicity. • OEHHA generally does not use a UF smaller than 10 when converting from a LOAEL to NOAEL for chronic endpoints, even when the effect is mild. For acute endpoints, a smaller UF may be justifiable, but for chronic effects this is problematic.	antibodies have been shown to be quite specific and are rarely detected at elevated levels in healthy patients (Kavanaugh et al., 2000; Wichainun et al., 2013). Therefore, the results from (Keil et al., 2009) do represent an adequate biomarker of autoimmunity, and the selection of $UF_L = 3$ is justified due to the observed effect being considered an early, subclinical or pre-clinical early marker of disease and the non-standard dose-response observed in the study.
BMR selection		
SACC	**SACC COMMENTS:** Recommendation: Provide better justification or reference policy to support the choice of BMR used in computing the BMDL. For liver, kidney, and male reproductive effects, 10% levels are used; the 1% level is used for the congenital heart defect and immunotoxicity. The extent to which this is driven by EPA policy should be explained in the document. A 1% response level could be supported, but more explanation is needed to ensure full transparency for the basis for this selection.	Selection of a lower BMR based on the severity of an effect (referred to in the Guidance as a "frank effect") is consistent with EPA BMD guidance (U.S. EPA, 2012a) and standard EPA practice. Considerations for BMD modeling are provided in Appendix G.
SACC	**SACC COMMENTS:** With a cumulative acute UF of 10 [(interspecies uncertainty factor, UF_A=3 (*i.e.,* extrapolating from laboratory animals to humans) and intraspecies uncertainty factor, UF_H=3 (*i.e.,* human [intraspecies] variability)], should not one of these be reduced to 1.0 based on the highly conservative nature inherent in use of a BMDL-0.01 level? These decisions are based on scientific judgment but require more	BMR selection is independent from uncertainty factor determination, which is based on confidence in the dose-response and how it accounts for variability and uncertainty between the assay and the human population. The use of a 1% BMR based on a severe effect does not

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	comprehensive justification.	indicate that variability between humans and animals or among the human population is reduced.
SACC	**SACC COMMENTS:** For cardiac malformations as a developmental effect of TCE exposure, a $BMDL_{01}$ value is calculated based on the seriousness of this adverse effect. While the explanation for using a 1% level is clear and agrees with standard practice, the use of these data from the Johnson et al. (2003) study raised concerns due to issues with the experimental design and replication problems.	A detailed justification for the use of a 1% BMR for (Johnson et al., 2003) is provided in Section 3.2.5.3.1. A re-run of BMD modeling was performed to confirm the results of the 2011 dose-response assessment and is presented in Appendix J.
99	**PUBLIC COMMENTS:** Using additional information reported by Johnson et al., EPA revaluated the BMR used in the 2014 risk assessment using biological and statistical factors, concluding "that the biological severity of the effect, potentially lethal heart defects, strongly supported a BMR of 1%." Compared to the 2014 assessment, EPA concluded that "the p-value of = 0.661 from the updated BMDS nested model run is significantly improved, demonstrating strong model fit and confirming the 2011 conclusion that the modeling results for cardiac malformation data are appropriate for reference value derivation."	
Meta-analysis of epidemiological cancer data		
SACC	**SACC COMMENTS:** • With two exceptions, members indicated that the short subsection on the meta-analysis for TCE-induced cancer is concise and clearly explains the interpretation of the conclusions of an association with kidney cancer, liver cancer, and NHL. This section and the analysis are clear and appropriate. The exclusion of Vlaanderen et al. (2013) is well discussed and justified. One member of the Committee had reservations about the association of TCE with liver cancer (due to conflicting evidence, appearance of tumors only at high doses, and potential MOA not relevant to humans). Because the POD is derived from the more definitive kidney cancer data and modified to account for additional cancer types (liver and NHL), the	All studies considered in EPA's cancer meta-analyses scored acceptable for data quality and passed inclusion/exclusion criteria for suitability of the data. Unacceptable studies were not considered for inclusion. All details on the data quality evaluation results for these studies are provided in supplemental files. EPA provides a meta-analysis stratified by data evaluation score in Appendix K.2.2.2 that demonstrates stronger statistical significance for each tumor type among high-quality studies compared to overall

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	other members of the Committee did not see this as an issue.	summary relative risks (RRs).
94	**PUBLIC COMMENTS:** EPA provides no discussion on the study quality details for individual studies in its meta-analysis and how they could have affected the validity of individual effect estimates/overall interpretation of results. The degree to which these methodological limitations may have impacted the individual effects estimates and interpretability of meta-analysis relative risk estimates (meta-RRs) needs to be further investigated by EPA.	
94	**PUBLIC COMMENTS:** EPA's conclusion that there are positive associations of NHL, kidney cancer, and liver cancer with exposure to TCE do not account for some serious methodological limitations of individual studies (*e.g.,* exposure measurement error and confounding), qualitative heterogeneity across individual studies (ratio measures, exposure measurements and contrasts, mortality vs. incidence data, and covariate adjustments), and unjustified adjustments in quality ratings, and the inappropriate removal of the largest study (Vlaanderen et al., 2013). These limitations are not fully captured through statistical modeling, which calls into question the appropriateness of meta-analyzing these results. The meta-analyses results are not reliable, and EPA's interpretation of the results is not appropriate. The meta-analyses do not support TCE as a risk factor for NHL, kidney cancer, or liver cancer.	
94	**PUBLIC COMMENTS:** EPA inappropriately used both inclusion/exclusion criteria and study quality criteria to determine which studies to include in the meta-analyses. Data quality criteria should be applied only to studies that have been selected for inclusion in the analysis. Data quality criteria were also inconsistently applied. For example: There is no explanation for excluding Bahr et al. (2011) (scored Unacceptable), but not Buhagen et al. (2016) (scored Low), when both studies met the inclusion criteria. This raises a question of the objectivity of the study selection process.	
94	**PUBLIC COMMENTS:** EPA changed the study quality rating for a few studies (*i.e.,* Vlaanderen	

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	et al., 2013; Buhagen et al., 2016; Bahr et al., 2011) after completing an evaluation based on the predetermined Data Quality. These rating changes were based on factors that had already been accounted for in the Data Quality Criteria. It is unclear whether the considerations for re-rating these studies were consistently evaluated in all of the included studies, or whether certain studies were singled out. As one example: Vlaanderen et al. (2013) was initially rated as a "High" quality study based on the Data Quality Criteria, but then re-rated as a "Medium" quality study due to 'potential JEM misclassification.' However, this should have been accounted for in Metric 4, where a "low" score was given. It is unclear why the same issue was double-counted in the rating. It is also unreasonable to re-rate the entire study (from "High" to "Medium" quality) for specific issues that should have been accounted for by simply re-rating individual aspects/metrics that contribute to the overall rating of the study. The objectivity and reasonableness of these are questionable, and likely affected the meta-analyses and results beyond individual study ratings.	
94	**PUBLIC COMMENTS:** Several studies in the meta-analysis with overall study quality ratings of "high" may have had serious limitations: • Exposure measurement errors: due to use of less-established exposure assessment methods, lack of method validation, or having limited employment information for job-matrix construction introduce information bias into the meta-analysis. • Limited exposure ranges (*e.g.,* not adequate for developing an exposure-response) introduce bias to the meta-RRs because their effect estimates are not adequate to fully capture the underlying association between exposure and cancer outcomes. • Confounding: studies rated "low" for covariate adjustment, covariate characterization, and co-exposure confounding. EPA should compare results of these studies with methodological limitations to results of the few studies without limitations in generating the summary effect estimates (*i.e.,* meta-RRs), particularly when	

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	stratifying by overall study quality, in order to assess the degree to which the methodological limitations may have impacted individual effects estimates and the interpretability of meta-RRs.	
94	**PUBLIC COMMENTS:** EPA considered all risk ratio measures (*i.e.,* RR, odds ratio [OR], hazard ratio [HR], standardized mortality ratio [SMR], and standardized incidence ratio [SIR]) as equivalent. Although this is not an uncommon approach for meta-analyses, it can introduce bias to results, especially when conditions where other ratio measures would mathematically approximate RR are not met in individual studies (*e.g.,* an OR from a case-control study that is not nested within an underlying cohort).	EPA considered all data from multiple studies within a single cohort in total, with the most updated cohort results used in the meta-analyses.
94	**PUBLIC COMMENTS:** In the meta-analyses, EPA included studies where a diversity of TCE exposure measurements were used. While this enabled a large number of studies to be included, an effect estimate based on one exposure measurement is not necessarily comparable to the effect estimate based on another exposure measurement.	EPA considered the best overall effect estimate for each study, along with stratifications for "high" vs "low" exposure.
94	**PUBLIC COMMENTS:** EPA abstracted effect estimates for contrasts within the study population and were either comparisons of groups exposed and not exposed to TCE or comparisons of groups with the highest and lowest level of exposure. However, the definitions of "exposed" vs. "unexposed" or "high" vs. "low" exposure levels were not specified and could be widely different between studies. Diversities in both exposure measurements and contrasts introduce heterogeneity across the meta-analyzed studies and hinders the interpretability of the meta-analyses results. Thus, the appropriateness of meta-analyzing these study results is questionable.	There is always uncertainty associated with study author classification of study groups, however EPA attempted to use consistent parameters when grouping studies.
94	**PUBLIC COMMENTS:** EPA inappropriately assumed that meta-RR estimates, which are based on RR estimates for both cancer mortality and incidence, were appropriate estimates for cancer incidence ratios. Survival rates for cancer generally depend on the cancer site and stage at diagnosis, mortality rates often poorly approximate incidence rates, particularly	The meta-analyses were based on associations with cancer incidence, not mortality.

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	when cancers are diagnosed at an early stage. Kidney cancer and NHL have high 5-year survival rates; therefore, mortality risk estimates are not good estimates for incidence risks for these two cancers.	
94	**PUBLIC COMMENTS:** The most fully adjusted risk estimate from each study was used in each meta-analysis in the draft risk evaluation. However, each study adjusted for a unique set of covariates, and even the same covariates were often defined and measured differently across studies. EPA's decision on whether fixed-effects or random-effects model results should be used to represent the summary effect estimates (*i.e.,* meta-RRs) solely relied on the I^2 statistic and visual inspection of the plotted effect estimates. This evaluation is not a replacement for understanding the underlying meanings of the values of the effect estimates. Given the heterogeneity between studies, qualitative evaluation of whether the effect estimates from individual studies can be considered as estimating the same underlying effect should be conducted along with the quantitative examinations. If this is done, it is evident that the fixed-effects TCE models, which assumed that each of the individual studies are estimating the same underlying effect, likely are subject to biased results as a result of this heterogeneity.	EPA's procedure for evaluating heterogeneity paralleled the methods from the peer-reviewed 2011 IRIS Assessment. EPA agrees that the random effects model is preferable in cases of significant heterogeneity and states, "random-effects models are consequently preferred to fixed-effects models due to the degree of heterogeneity" in Section 3.2.4.2.1.
94	**PUBLIC COMMENTS:** EPA used a "leave-one-out" approach in the assessment of influential studies (*i.e.,* conducted each analysis several times, removing one study each time) in fixed-effects, but not random-effects, models for NHL, kidney cancer, and liver cancer. In doing so, EPA identified only Vlaanderen et al. (2013) as an influential study; meta-RRs largely remained not statistically significant with the removal of any other study. It is not clear why EPA only used fixed effects models for the "leave-one-out" analysis when random-effects models are more appropriate for these data given indications of heterogeneity. EPA's reason for omitting Vlaanderen et al. is flawed. • Just because the value of I^2 statistic was substantially reduced, does	The data quality of (Vlaanderen et al., 2013) was not downgraded based on meta-analysis determinations, it was merely omitted from sensitivity meta-analyses because it was shown to have overly large influence on the results due to large sample size and likely low sensitivity for detecting effects (see Section 3.2.4.2.1). The meta-analyses plots presented with exclusion of (Vlaanderen et al., 2013) present an updated I^2 score that is reduced, indicating reduced heterogeneity and mitigating the need for use of

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	not mean that there is no underlying qualitative heterogeneity among the remaining studies. • Using this reasoning for downgrading the study quality once again to support the omission, without acknowledging the many methodological strengths and the overall good quality of the study is not justified. • The next largest studies with the highest influences on the meta-RRs had similar methodological limitations and their initial study ratings were worse, and therefore, they are likely more subject to bias. An important question is whether the effect estimates from Vlaanderen et al. (2013) or any other study under review can be considered as estimating the same underlying effect. This was not considered.	the random effects model. Omission of (Vlaanderen et al., 2013) was only one sensitivity analysis conducted in supporting EPA's conclusions.
94	**PUBLIC COMMENTS:** Stratification of meta-analysis by study quality showed that "For all three tissues, the meta-RR was greater among the high-quality studies compared to medium or low-quality studies." It is worth noting that this finding is likely sensitive to the quality rating of Vlaanderen et al. (2013). Had this study not been re-rated from "High" to "Medium" quality, the meta-RR would likely have been greater among the medium- or low-quality studies compared to the high-quality studies, which would have led to a completely different conclusion.	The study was not "re-rated." All data evaluations are subject to expert judgment adjustments to the overall score, and it is likely that similar considerations influenced the manual downgrade and the reduced sensitivity of the study in the meta-analysis.
94	**PUBLIC COMMENTS:** There was a blatant misuse of funnel plots in the draft risk evaluation to assess publication bias. EPA used funnel plots to visually examine a comparison of study size and effect size with and without the Vlaanderen et al. (2013) study. This represents a fundamental misunderstanding of funnel plots, which are crude measures of whether studies represent a bias in terms of positive results, and should not be used to determine the sensitivity of meta-analyses to a particular study.	The funnel plots were presented to demonstrate publication bias both for the overall meta-analyses, and for the sensitivity analysis involving omission of the (Vlaanderen et al., 2013) study. They were not intended to determine the sensitivity of the performed meta-analyses.
94	**PUBLIC COMMENTS:** The Draft supports the 2011 IRIS assessment classification of TCE as "Carcinogenic to Humans," but fails to discuss or recognize that such classification is inconsistent with a definitive report by the National	The NAS review on TCE human health risks was published in 2006 (NRC, 2006), prior to both the IRIS Assessment and the publication

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	Academy of Sciences (NAS). • This classification is appropriate only when there is convincing epidemiologic evidence of a causal association between human exposure and cancer, or several conditions are met with other lines of evidence. • Neither the epidemiological data nor animal studies meet the threshold for classification as carcinogenic to humans. • Based on an analysis by Gradient of the new meta-analyses of TCE and on NHL, kidney cancer, and liver cancer risks, the meta-analyses results are not reliable, and EPA's interpretation of the results is not appropriate. The evidence of an association with cancer is neither "convincing" or "strong." The classification of TCE as "Carcinogenic to Humans" is not supported by the evidence or justified under the 2005 Guidelines. Risk estimates from individual cohort studies, and the meta-estimates based on these studies, likely did not properly reflect the true associations between TCE and these cancers.	date for many of the studies included in the meta-analyses. Therefore it is missing many studies that were covered by EPA's analysis in the 2011 IRIS Assessment (U.S. EPA, 2011e), 2014 Workplan Risk Assessment (U.S. EPA, 2014b), and this Risk Evaluation. Furthermore, the confirmation of statistically significant summary effect estimates across a large group of studies in all three cancer types as well as positive results in animal cancer bioassays is very strong support for the conclusion that TCE is "Carcinogenic to Humans."
105	**PUBLIC COMMENTS:** EPA conducted meta-analyses of epidemiological cancer data and found consistent positive associations for multiple cancer sites, and appropriately used the cancer dose response characterization from EPA's 2011 IRIS assessment (U.S. EPA, 2011). In light of this, the executive summary and the body of the document should clearly state the conclusion that TCE is "carcinogenic to humans." This was the conclusion in the IRIS assessment and the draft risk evaluation shows that the evidence since then has strengthened.	EPA agrees with this comment and the risk evaluation has been updated accordingly.
Evaluation of animal cancer data		
SACC	**SACC COMMENTS:** The Committee was unclear of the meaning of the justification of "confounding mortality" used to score the NCI (1976) female study on kidney endpoint as unacceptable (p. 211, lines 775-776).	The following clarifying language has been added to the Risk Evaluation: "due to high mortality in control mice and rats as well as long post-exposure period prior to sacrifice that could

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		have allowed for recovery…"
SACC	**SACC COMMENTS:** Recommendation: Clarifications and corrections are needed. • Section 3.2.3.2-Genotoxicity and Cancer Hazard, p. 218: Improve the discussion to clarify the sex-dependent differences in cancer incidence, especially for kidney and liver.	EPA does not believe that sex-specific difference in cancer incidence for non-reproductive organs are relevant for this assessment except for consideration of certain mode of action (MOA), which are discussed in Section 3.2.4.2.2.
94	**PUBLIC COMMENTS:** EPA seems to overly discount negative animal carcinogenicity data and to highlight marginal findings. • EPA's conclusion that kidney cancer is evident in rats rests on one statistically significant finding in over 70 dose/tumor endpoint comparisons and references to exceedances of historical control values. • EPA's conclusion that TCE is a known kidney tumorigen is based on flawed studies and not warranted. The data are inconsistent and do not meet the criterion of "extensive evidence of carcinogenicity in animals." Several marginal findings do not constitute "extensive evidence."	EPA disagrees with this statement, and positive animal bioassays are consistent with results from various epidemiological results, including a meta-analysis for each of the three primary tumor types assessed.
Genotoxic MOA for cancer		
SACC	**SACC COMMENTS:** Recommendation: Include a table summarizing what is known on the genotoxicity of TCE and metabolites. • The Committee noted that the MOA for TCE carcinogenicity is not well addressed in the draft risk evaluation, because it relies on the conclusions from the IRIS assessment. The risk evaluation should include a table of data addressing the genotoxicity (for both *in vivo* and *in vitro* studies) of TCE and metabolites. Because kidney cancer is the most important driver of the conclusions, the data for this tissue should be prioritized.	EPA has added a table of data extraction and evaluation for all identified genotoxicity studies on TCE and important metabolites as a supplemental file.
SACC	**SACC COMMENTS:** The Committee noted that a genotoxic mechanism (supportive of using a	EPA has improved the discussion of cancer

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	linear non-threshold [LNT] model) had been assumed for TCE. There is some support for this due to the mutagenic potential of the metabolites S-(1,2-dichlorovinyl)-L-cysteine (DCVC) and S-(1,2-dichlorovinyl) glutathione (DCVG). While this evidence is greatest with regard to kidney toxicity and is further supported by relevant data from female reproductive toxicity, it is far from definitive. Committee members were concerned with both the low mutagenic potential of these metabolites and the doses that would be achievable *in vivo*. It is probably best to consider the presence of these compounds as providing "biological plausibility" for a genotoxic mechanism and consistent with an LNT model rather than conclusive proof. However, there is also no compelling evidence for other mechanisms, so no reason to specifically reject a genotoxic mechanism.	MOA in Section 3.2.4.2.2. Improvements include more detailed discussion and consideration of other mechanisms. Overall, the MOA conclusions are not changed, and EPA determined that TCE exhibits a genotoxic mode of action that is supported for kidney cancer while any particular MOA cannot be concluded for the other tumor types. Some additional discussion of the uncertainty associated with GSH metabolism across humans has been added.
108, 99	**PUBLIC COMMENTS:** EPA appropriately concludes that TCE is genotoxic, stating "there is sufficient evidence that TCE-induced kidney cancer operates primarily through a mutagenic MOA." The conclusion regarding a lack of evidence for alternative MOAs is also consistent with other findings of authoritative agencies.	
62	**PUBLIC COMMENTS:** The data in Yoo et al., 2015 (Health and Environmental Research Online [HERO] ID 2799570; PMID: 25424545; PMCID:PMC4281933) and Luo et al., 2018 (PMID: 29190187; PMCID: PMC6088749), together, strengthen the plausibility of the mutagenic MOA for TCE-induced kidney cancer – initiation through DCVC mutagenicity followed by promotion through compensatory cell proliferation that may be due to the effects of both DCVC and TCA. EPA should add this information to strengthen the conclusions for a mutagenic MOA for kidney cancer.	
63	**PUBLIC COMMENTS:** The new and analytically robust data showing that glutathione-conjugate derived metabolism is a very minor metabolic pathway of TCE in rats and humans challenge the hypothesis that this pathway is plausibly consistent with a mutagenic MOA in rodents and humans.	

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94	**PUBLIC COMMENTS:** A role for glutathione conjugate-derived metabolites in TCE kidney toxicity and cancer risk assessment should be reconsidered. There is compelling evidence that the glutathione (GSH) conjugation pathway is an extremely small contributor to TCE metabolism. • Yoo et al. (2015) demonstrated that DCVG and DCVC were only a small fraction of total metabolites quantitated in kidney. Trichloroethanol (TCOH) kidney concentrations were 2- to 4-fold greater than TCA; TCA concentrations were 100- to 1,000- fold greater than DCA; and DCA concentrations were 100- to 1,000-fold greater than either DCVG or DCVC, resulting in the conclusion that TCE oxidative metabolism was up to five orders of magnitude greater than glutathione conjugate-derived metabolism. These findings are consistent with Kim et al. (2009) and supported by Luo et al. (2018) and questions the role of the GSH conjugation pathway in the kidney cancer MOA. Estimated levels of DCVC and its reactive metabolites in kidneys of TCE-exposed mice are insufficient to account for toxicity (see Yoo et al., 2015, Green et al., 1997, and Luo et al., 2018).	
Alternative MOAs for cancer		
SACC	**SACC COMMENTS:** Some Committee members suggested that alternative MOAs for TCE in liver carcinogenesis have not been adequately discussed. Multiple MOAs have been proposed for the carcinogenic action of TCE and its metabolites in rodents, including activation of peroxisome proliferator activated receptor alpha (PPARα). The human relevance of PPARα agonism has been the subject of debate due to the substantial species differences in response to peroxisome proliferator receptor activation between rodents and primates, with rodents, especially mice, showing greater sensitivity than primates. A Committee member suggested that other, non-PPARα mechanisms, such as cytotoxicity and activation of other nuclear receptors had not been adequately discussed.	EPA has added an additional subsection on polyploidization. EPA has additionally expanded the discussion of PPARα and cytotoxicity/reparative hyperplasia.
SACC	**SACC COMMENTS:**	

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	Recommendation: Clarifications and corrections are needed. • Section 3.2.4-Weight of Scientific Evidence, p. 220, lines 1170-1174: Regarding the MOA for liver cancer, the consensus is that while peroxisome proliferation in rodents is well-established, it is not relevant to humans. This point should be noted here.	EPA disagrees with this statement. The significance of the PPARα pathway in humans is debated, and while it may be less active it is not necessarily irrelevant.
SACC	**SACC COMMENTS:** Recommendation: Clarifications and corrections are needed. • Section 3.2.4.2.2-Mode of Action: Kidney Cancer, p. 227: The document states the following: "the predominant mode of action (MOA) for kidney carcinogenicity involves a genotoxic mechanism." Although the next paragraph also discusses alternative MOAs, which include cytotoxicity and dysregulated injury and repair cycles, the relative importance of each mechanism and the evidence supporting each mechanism are not appropriately described.	EPA has improved the discussion of cancer MOA in Section 3.2.4.2.2. Improvements include more detailed discussion including addition of some recommended citations and consideration of other mechanisms. Overall, the MOA conclusions are not changed, and EPA determined that TCE exhibits a genotoxic mode of action that is supported for kidney cancer while any particular MOA cannot be concluded for the other tumor types. The SACC directly refuted written and oral comments citing Zhang et al, 2018 (available at https://www.sciencedirect.com/science/article/pii/S0378427418314905) suggesting that the assay methods used in the 2011 PBPK model for measuring DCVG were inappropriate or gross overestimations.
62	**PUBLIC COMMENTS:** It is surprising that PPARα activation is elevated in the draft when it has been concluded by IARC that there are a number of other equally plausible mechanisms. Rusyn et al. (2014) indicates that "TCE and its oxidative metabolites have been shown to induce several non-genotoxic effects that may contribute to hepatocellular tumors. These include epigenetic alterations; cytotoxicity and secondary oxidative stress; alteration of proliferation and apoptosis, and clonal expansion; and PPARα activation," and that "several data gaps reduce the confidence in the conclusion that TCA induces hepatocarcinogenesis solely through a PPARα-activation mechanism." EPA should not provide specific emphasis on PPARα activation as among the "strongest" potential mechanisms for liver cancer induced by TCE and instead more directly state that multiple MOAs may be responsible for liver cancer effects of TCE.	
103	**PUBLIC COMMENTS:** EPA should fully evaluate and discuss the plausibility of the alternative cancer MOA and weigh the scientific evidence of this alternative approach as part of the risk characterization.	

	• EPA should utilize an established framework to organize evidence for MOA based on side-by-side WOE comparison of alternative plausible MOAs. • EPA is obligated to calculate potential risks from alternative plausible MOAs, and the default option, and to characterize each fully, both narratively and quantitatively, for the risk manager.	
103, 94	**PUBLIC COMMENTS:** MOA analysis should be updated to include additional studies: • Zhang et al. (2018): This study identified the potential for the GSH metabolite pathway, which EPA identified as a potential MOA for kidney cancer, to be overestimated if the non-specific difluoronitrobenzene derivatization analytical method is used. EPA should reconsider whether this quantitatively changes the kidney cancer risk attributed to TCE exposure. • Studies conducted with structurally similar perchloroethylene that is metabolized to structurally similar compounds through identical metabolic pathways. • Luo et al. (2018), reported that for TCE, concentrations of metabolites formed by oxidative biotransformation were several orders of magnitude higher than concentrations of metabolites formed by the GSH pathway, suggesting a lack of support for the conclusion that the GSH metabolites are responsible for TCE-induced kidney tumors in rodents. • Transcriptomic studies including Zhou et al. (2017); Cichocki et al. (2017), and Venkatratnam et al. (2017). The latter two suggest that PCE and TCE exposure are associated with PPAR-α, which indicates that these findings may not be relevant to humans. The current available scientific information is not consistent with the conclusion that the MOA for TCE-induced kidney cancer in rats involves DNA-reactive metabolites from the GSH conjugation pathway as a key event. EPA needs to incorporate the evidence from these recent studies into the TSCA draft risk evaluation for TCE and produce alternative cancer toxicity values based on a threshold approach.	

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94	**PUBLIC COMMENTS:** EPA has failed to include any of the more recent published studies that undermine the validity of EPA's assumptions in the estimation of human kidney toxicity and cancer risks including Zhang et al. (2018)	
Linear extrapolation for cancer dose-response assessment		
SACC	**SACC COMMENTS:** Although following an LNT dose-response model for cancer assessment would seem to follow standard practice, support for it remains weak. • Two caveats here that should be considered: While the TCE metabolite DCVC is clearly mutagenic, it is a relatively weak mutagen, and while there is evidence that mutagenicity does play a role, it is clearly not the only MOA. Moreover, its relative contribution as compared to cytotoxicity and proliferation is unclear.	EPA provides multiple lines of justification for its application of LNT dose-response model, in addition to the assumed genotoxicity of kidney cancer (Section 3.2.4.2.2). Application of this model is consistent with EPA Guidelines for Carcinogen Risk Assessment.
108, 99	**PUBLIC COMMENTS:** There is agreement with EPA's justification in adopting a linear, no-threshold approach for TCE carcinogenicity. • There is strong support for TCE's cancer classification and a mutagenic MOA. EPA correctly concludes that TCE is linked to NHL, kidney, and liver cancer. • EPA's decision to affirm TCE's carcinogenicity and carry forward cancer hazard for dose-response modeling is wholly consistent with numerous other classifications. • EPA's conclusion in the draft is also aligned with EPA's 2014 Work Plan Chemical Risk Assessment of TCE as well as the recent 2019 ATSDR toxicological profile of TCE. • There is support for EPA's decision to adhere to the *EPA Guidelines for Carcinogen Risk Assessment* and use the approach of linear non-threshold extrapolation in the cancer risk modeling for TCE, indicating that this is the most scientifically sound and health-protective approach in cancer dose-response modeling for TCE. • Even were the evidence deemed insufficient to identify with certainty a genotoxic MOA, there is longstanding EPA policy guidance and precedent supporting a default to a no-threshold, linear extrapolation	

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	method for cancer dose-response modeling.	
108	**PUBLIC COMMENTS:** EPA must employ health-protective approaches to dose-response modeling. The National Research Council's report, *Science and Decisions: Advancing Risk Assessment* discusses the need to conduct a linear extrapolation at the population level, even where a threshold might theoretically exist indicating that: • "Human variability with respect to the individual thresholds for a nongenotoxic cancer mechanism can result in linear dose-response relationships in the population." • "In the laboratory, nonlinear dose-response processes … may be found to cause cancer in test animals. However, given the high prevalence of these background processes, given cancer as an end point, and given the multitude of chemical exposures and high variability in human susceptibility, the results may still be manifested as low-dose linear dose-response relationships in the human population." • The 2016 amendments to TSCA made explicit and strengthened EPA's obligation to consider risks to and protect subpopulations that may be more exposed or more susceptible to the effects of chemical exposure than the general population. To meet this statutory requirement, EPA must use a linear non-threshold modeling approach. Given: (1) existing EPA guidance, (2) the many sources of variability in the human population, (3) TSCA's mandate to protect "potentially exposed or susceptible subpopulations," and (4) the clear presence of individuals with preexisting health conditions, metabolic or genetic variability, or other factors that make them more susceptible, the use of the linear extrapolation is the only appropriate option for cancer dose-response modeling. EPA also must use this approach comply with EPA's duty to consider the "best available science" under TSCA.	
99	**PUBLIC COMMENTS:** Building on previous determinations, and following the guidelines, the	

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	draft risk evaluation has correctly determined that TCE is a genotoxic carcinogen and that hypothesized MOAs that assume a threshold are unsupported. At the SACC meeting, some industry presenters urged EPA to base cancer risk estimates on a non-linear MOA. A non-threshold linear extrapolation is the correct approach to estimate risk.	
94	**PUBLIC COMMENTS:** Cases have been made that the scientific foundations of the linear non-threshold single-hit model are seriously flawed due to default assumptions and policy-based analytic procedures. These include: • Weight vs. surface area; maximum or average likelihood vs. upper 95% confidence; malignant tumors vs. malignant plus benign tumors; average animal sensitivity vs. most sensitive; pharmacodynamics vs. effective dose; and risks at shorter than equilibrium buildup time. • Using alternatives could result in a reduction in risk estimates. To demonstrate that this approach constitutes "best available science" EPA should consider these criticisms and evaluate the appropriateness of assuming a linear non-threshold model on a case-by-case basis.	
94	**PUBLIC COMMENTS:** It should be noted that in characterizing the upper confidence limit value generated by the current methodology, EPA does not refer to the impact on the risk estimate of the policy chosen dose-response model, the linearized multistage model (LMS). Alternative models would give risk values several orders of magnitude lower than the LMS model.	
Derivation of the IUR		
99	**PUBLIC COMMENTS:** EPA's overall conclusions of a mutagenic MOA for TCE-induced kidney cancer were consistent with conclusions in the 2011 IRIS assessment; therefore, EPA utilized the same IUR and oral slope. EPA examined non-linear MOAs but correctly concluded that although the WOE also supports involvement of processes of cytotoxicity and regenerative proliferation in the carcinogenicity of TCE, data were lacking and the support was not as strong as a mutagenic MOA. EPA indicated that any possible involvement of a cytotoxicity MOA would be	EPA followed the peer-reviewed process for cancer dose-response analysis developed in the 2011 IRIS Assessment, including using the IUR for (Charbotel et al. 2006) and adjusting based on relative risk for other tumor types. (Charbotel et al. 2006) received a High in EPA's data quality evaluation and the meta-analysis concluded that the epidemiological database

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	additional to mutagenicity, and the dose-response relationship would nonetheless be expected to be linear at low doses. Therefore, the additional involvement of a cytotoxicity MOA does not provide evidence against the use of linear extrapolation from the POD. The final evaluation should retain the unit risks in the draft.	supported an association between TCE exposure and kidney cancer as well as the other two tumor sites. EPA has discussed uncertainty in the cancer dose response based on adjustment of the IUR for all three tumor sites in Section 3.2.6.4 and acknowledges that it likely represents an upper bound value, however differences from the true value are unlikely to vary by more than ~2-fold.
94	**PUBLIC COMMENTS:** Based on the new meta-analysis with epidemiology studies on kidney cancer risk, TCE is not a risk factor for kidney cancer; therefore, it is not appropriate to derive the IUR using Charbotel et al. (2006), which only investigated RCC. The study's author concluded that the study only "suggests that there is a weak association between exposures to TRI [TCE] and increased risk of RCC," which is not supportive of a robust relationship. Problems with Charbotel et al. (2006): • The study has evidence of misclassification of exposure and confounding from cutting fluid exposure, resulting in considerable uncertainty in the outcome. • Methodological limitations include attrition bias, small sample size, and limited confounder adjustment. • Selection bias: the study selected controls among patients of the same urologist or general practitioner as the cases. These controls might have systematically higher or lower odds of TCE exposure than the underlying true base population that gave rise to the cases, thus biasing the study results. • All participants of Charbotel et al. (2006) resided in a particular geographic area they may share certain characteristics that limit the generalizability of study results to other populations. EPA should follow the recommendation of the NAS, which indicated there was insufficient epidemiologic data to support quantitative dose-response modeling for TCE and cancer.	
94	**PUBLIC COMMENTS:** There are serious concerns about the scientific appropriateness of adjusting the IUR derived from kidney cancer data to account for NHL and liver cancer because epidemiology data are not sufficiently robust to	

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	allow such calculations and the data that are available indicate that the IUR for kidney cancer is protective for all three cancer types. The RR estimates from the 2011 IRIS meta-analyses do not accurately reflect the relative contributions from different cancers.	
94	**PUBLIC COMMENTS:** In an alternative approach to the IUR calculation, EPA relied on SIRs for kidney cancer, liver cancer, and NHL reported by Raaschou-Nielsen et al. (2003) to calculate extra cancer risks. Because only SIRs were assessed in this study, key confounders for liver cancer, such as smoking, heavy alcohol consumption, and chronic viral hepatitis, and kidney cancer confounders like smoking and body mass index, were not adjusted for. Therefore, the SIRs from Raaschou-Nielsen et al. (2003) should not be used in a regulatory human health risk assessment.	
94	**PUBLIC COMMENTS:** There are considerable uncertainties in the quantitative analyses in which EPA adjusted the IUR estimate for multiple cancer sites. • For the approach using the meta-RR estimates, EPA assumed that populations of the underlying studies in the meta-analyses had similar TCE exposures. This assumption was likely not true, as the underlying epidemiology studies were conducted in different counties, industries, and time periods. • Diagnosis and classification of NHL have changed over time; this likely led to errors in outcome ascertainment in epidemiology studies. It is difficult, however, to estimate the direction and extent of this bias. • Uncertainties in exposure assessment and confounder adjustments in Raaschou-Nielsen et al. (2003), undermining the validity of the RR estimates reported in this study. • EPA did not acknowledge that the assumption that lifetime background incidence rates for each cancer site in the U.S. general population proportionally approximate the age-specific background incidence rates in the study populations likely does not hold, because the epidemiology study populations, generally consisting of workers	

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	with occupational exposure to TCE, often differed from the U.S. general population with regard to several lifestyle factors such as smoking, obesity, and socioeconomic status. These factors could have impacted the background cancer incidence rates in worker populations, making them different from the background rates in the U.S. general population. • EPA assumed that the dose-response relationships for NHL and liver cancer were similar to the linear one for kidney cancer; however, because of the use of dichotomous exposure in the underlying data, it is not possible to know with any degree of confidence that the dose-response relationships for NHL and liver cancer are linear. • EPA failed to acknowledge the assumption that the dose-response between TCE exposure and NHL and liver cancer would yield the same POD as that of kidney cancer. Even if NHL and liver cancer had identical dose-response curves as kidney cancer, which is unlikely, the PODs based on 1% extra risks of NHL or liver cancer would be different from that of kidney cancer because these cancers have different incidence rates in the general population. EPA did not demonstrate that any potential risks of kidney cancer, NHL, or liver cancer from TCE exposures are additive. Even if all three cancers were causally associated with TCE exposure, and had identical dose-response relationships, both of which are highly unlikely, this does not necessarily mean effects were additive.	
99, 108	**PUBLIC COMMENTS:** Rather than summarily dismissing acute cancer risks because they are harder to estimate, EPA should have quantified these risks using the framework outlined by the National Research Council (NRC), which reflects the best available science.	
PBPK model/dose metric and/or cross-species scaling approach		
SACC	**SACC COMMENTS:** Recommendation: Better discuss/justify the selection of each selected dose metric. • The text lacks transparency relative to the basis for selection of dose	Some language has been added to section 3.2.5.3.2 justifying use of oxidative metabolites based on data from (Buben and O'Flaherty,

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	metrics, and a number of questions remain to be answered. For example, how strong is the evidence that liver effects are driven by a metabolite? Is it merely that early studies show diminution of hepatic effect with a cytochrome P450 (CYP) inhibitor and enhancement with CYP inducers? Is this evidence particularly strong? Does this evidence clearly indicate that it is an oxidative CYP metabolite versus some other pathway? This might be a relatively straightforward discussion relative to the liver. However, the basis for this assumption relative to neurotoxicity, male reproductive toxicity, or congenital heart defects (only oxidative, not total metabolism?) is not clear. The short, vague statements in the text such as evidence suggests a metabolite important or the like, lacks detail and, therefore, lacks adequate transparency. An enhanced discussion should be provided in the text and in the uncertainty discussions. For example, if a single metabolite is responsible for an effect, is it truly best to use total metabolite as the dose metric? Would that not introduce more uncertainty than using parent compound, for example? What if the critical metabolite is a minor metabolite and the PBPK parameter TotMetabBW34 is overwhelmed by non-relevant metabolites? • One Committee member suggested that the risk evaluation might look to using the PBPK model as a more scientific approach to extrapolating long-term (chronic) exposures from short-term (acute) exposure data than extrapolating using Haber's Law that multiplies the exposure concentration (c) by the duration time (t) of exposure.	1985). In that study toxicity was linear with total urinary metabolites (and changing kinetics suggest consistent effects of metabolites even as parent TCE plateaus). General language justifying the use of TotMetabBW3/4 and AUCBld was added to Section 3.2.5.3. Uncertainties surrounding dose metric selection are covered in Section 3.2.6.2. There is too much uncertainty to extrapolate from acute to chronic exposure data. EPA does not use Haber's rule for acute to chronic exposures, only for adjusting hours/day or days/week exposure. EPA did use the PBPK model to provide additional occupational HEC/HEDs for the two key acute and chronic immunotoxicity studies.
SACC	**SACC COMMENTS:** Recommendation: Discuss why the PBPK model could not be used to examine a dose metric of total absorbed dose of parent TCE for the Selgrade and Gilmour (2010) study. • It was not clear to some Committee members why this was not done. If the toxicity is due to the parent compound, then this is the most appropriate dose metric. Moreover, because the level of any metabolite must be in some way proportional to the delivery of	Data from (Selgrade and Gilmour, 2010) has been run through the PBPK model and PBPK model outputs have replaced the previous HEC/HED values that were used in the draft risk evaluation. Based on other immune effects, TotMetab3/4 is the selected dose metric based and AUCBld is the alternative dose metric,

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	parent compound, then this would still be a potentially valuable dose metric. The decision to not use this or similar dose metric should be described.	which is similar to total absorbed dose. EPA additionally used the PBPK model to derive HECs/HEDs for occupational exposure for the two key acute and chronic immunotoxicity studies.
SACC	**SACC COMMENTS:** Although it is not stated in the text, presumably the HEC determination from Selgrade and Gilmour (2010) is based on the reference concentration (RfC) methodology assuming TCE is a category 3 gas. This should be explicitly stated. • Based on the partition coefficient of TCE, it is not clear whether in short-term exposure the whole body is in steady state (likely not) and it is not clear the extent to which TCE is recirculated in the venous blood (thus limiting respiratory tract uptake). Thus, it is not clear that the standard chronic RfC category 3 assumption is valid. • Because a PBPK model is available and validated (according to the document), it is unclear why simulations are not performed to determine if the category 3 assumption is valid. • Methods used for cross-species scaling should be more prominent in the text rather than in the footnotes of a table.	
SACC	**SACC COMMENTS:** Recommendation: Expand the discussion on the PBPK model, including results of sensitivity analyses to identify key inputs. • The discussion of PBPK modeling and its use in dose-response assessments is too limited and lacks sufficient clarity for most readers to understand what this model is and how it can be used to reduce uncertainty relating external chemical exposure to internal (*i.e.,* blood and target tissue) doses, and in turn to the extent of injury. • Point out the large number of PBPK models and the inordinate time and effort expended by many scientists to develop the present version. • Expand description to include the basic model structure and key input parameters, including physical/chemical properties and physiological and biochemical indices. Add a table listing the parameters and referencing the sources of the values. Describe the	Additional discussion has been added throughout Section 3.2.2.5, however the model structure was already provided in Figure 3-4 and a high-level introduction to PBPK modeling was provided in the first few paragraphs of the section.

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	utility of PBPK models in route-to-route, species-to-species, high-to-low dose, duration-to-duration, and human-to-human extrapolations. • Emphasize that validated animal and human PBPK models allow one to make scientifically based predictions of target tissue doses of the toxicologically active form of TCE to monitor (*i.e.,* the dose metric). A clear explanation should be given of how the PBPK model is used to predict/simulate the exposure conditions required to produce the same blood or target tissue dose in animals and humans by outlining the basic steps. • Sensitivity analyses are frequently conducted with PBPK models to determine how much impact variance in each input parameter has on model output/simulations. Sensitivity analysis of models facilitates identification of factors, including personal characteristics, that have the largest impact on systemic deposition and adverse effects in organs of interest. This method of analysis allows researchers to learn how characteristics of different individuals or subpopulations may influence internal dosimetry, and in turn their susceptibility to particular chemical health effects.	
SACC	**SACC COMMENTS:** The draft risk evaluation assumes that the same tissue chemical level/ concentration will cause the same degree of injury in each species. It was not clear to all Committee members that this assumption is valid for all metabolites.	This uncertainty is accounted for by the 3x component of UF_A that accounts for toxicodynamic variation and uncertainty. The PBPK model can only account for toxicokinetic differences.
SACC	**SACC COMMENTS:** Recommendation: Discuss TCE metabolites in more detail including available evidence on links from metabolites to fetal heart malformations. • The draft risk evaluation notes that TCE metabolites, not the parent compound, are suspected as being responsible as the causative agent for fetal heart malformations. The PBPK model used in the EPA draft risk evaluation can be used to model the effects of TCE metabolites such as chloral hydrate, TCOH, trichloroacetic acid,	The consistent positive findings demonstrating developmental cardiac effects with TCA and DCA suggest that oxidative metabolism is important for TCE-induced heart malformations. All relevant studies are described by the WOE analysis in Appendix F.3.

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	dichloroacetic acid, and others. The experiments by Dawson et al. (1990, 1993) and Johnson et al. (2003), were not specific or definitive as to the responsible metabolite(s). The risk evaluation should provide additional information on all metabolites modeled and discuss the available evidence on the link from metabolites to fetal heart malformations.	
SACC	**SACC COMMENTS:** Recommendation: Include more discussion on uncertainties in the PBPK model and with route-to-route extrapolation from oral to inhalation. • The cited section (3.2.6) inadequately addresses the uncertainties/ data limitations of PBPK modeling approaches. Toxicity data from oral exposures are treated as equivalent with data collected from inhalation exposures, ignoring the uncertainties inherent when conducting route-to-route extrapolation, even when using a PBPK model. One Committee member suggested that EPA re-evaluate the relevance and quality of toxicity data based on route of exposure. It is not clear that pathways of exposure in key animal studies are appropriate for human extrapolation. Is greater weight given to inhalation studies? Is absorption, distribution, metabolism, and excretion different for inhalation and oral exposures and could this explain the differences between fetal heart malformation and immunosuppression findings? There are sufficient data on TCE to allow proper assessment of health endpoints via inhalation.	EPA has added a statement to Section 3.2.6.2. indicating that despite the model being peer reviewed and the selection of dose metrics that minimize uncertainties in route-to-route extrapolation, "there is likely to be remaining unaccounted uncertainties associated with route-to-route extrapolation as opposed to relying on data from the same exposure route as is being assessed." Despite this uncertainty, EPA relies on the peer-reviewed PBPK model for adequately deriving equivalent internal dose estimates via either inhalation or oral routes.
SACC	**SACC COMMENTS:** Recommendation: Consider breathing rates, alcohol consumption and other models for vapor generation in the inhalation assessment. Heavy alcohol consumption is known to interact and aggravate some of the symptoms of TCE exposure. Workers who consume alcohol on a regular basis, before or after they're exposed to TCE constitute a vulnerable sub-population.	In response to SACC and public comments, EPA used the PBPK model to derive HECs/HEDs for occupational exposure for the two key acute and chronic immunotoxicity studies. These model outputs accounted for elevated breathing rate of workers compared to the default at-rest assumptions of the model. The
56,	**PUBLIC COMMENTS:**	

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108, 100	EPA gives insufficient consideration of potential elevated respiration rates in exposed workers. EPA states that it expects that variability in human physiological parameters (*e.g.,* breathing rate, body weight, tidal volume), which may affect internal delivered concentration or dose, is sufficiently accounted for in the PBPK model although some differences among lifestages or between working and at-rest individuals may not have been accounted for. • EPA does not state the basis of this expectation or identify precisely which "differences . . . between working and at-rest individuals" are not considered in EPA's model. • The use of HEC99/HED99 (99th percentile for human equivalent dose [HED]) values is expected to account for the vast majority of physiological differences among individuals. • It is unclear whether the PBPK model sufficiently addresses potential elevated respiratory rates in workers. • Workers are a crucial vulnerable subpopulation with respect to TCE, and EPA must therefore fully and accurately characterize and account for potential elevated respiratory rates among active workers. EPA should not use a resting breathing rate for workers, but rather an exercise breathing rate, or at least something in between the two. • The recent National Academies of Sciences, Engineering, and Medicine (NASEM) Review of DOD's Approach to Deriving an Occupational Exposure Level for TCE, the NAS highlighted that all PBPK-based derivations of HECs performed using resting ventilation and associated cardiac output physiological profiles may be appropriate for clerical or other office workers (*e.g.,* vapor intrusion within an office building), but for other occupations where ventilation and cardiac output are elevated by more strenuous exertion for extended durations, resulting HECs may not be protective. • For workplace exposure cases, the committee recommended incorporating exercise (work) physiology and realistic durations from	derived occupational HEC/HED values are provided in Section 3.2.5.4.1, and they were used for occupational risk estimates instead of the default PBPK outputs that were used in the draft risk evaluation. Alcoholism has been added as a PESS factor in Section 3.2.5.2, especially in the context of increased susceptibility due to enhanced CYP2E1 expression. EPA identified both workers and ONU as a PESS in Section 2.3.3.

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	actual job profiles into PBPK simulations for selected end points most likely to drive the observed effect level. EPA is charged with examining the risks to workers in addition to clerical or other office workers. If EPA did use resting cardiac profiles, this analysis must be enhanced to provide more realistic estimates of exposure levels for active workers. If EPA used respiration rates appropriate for active workers, this should be clearly communicated.	
100	Pregnant workers are faced with several physiological burdens, including elevated cardiac output, heart rate, oxygen consumption, and total air moved in and out of the lungs, all of which can increase TCE exposure to the developing fetus. In order to adequately assess risk to the developing fetus, EPA must take these factors into account and employ PBPK models that reflect exposure burden in the fetal compartment.	There is no available PBPK model that accounts for a fetal compartment. EPA believes that use of 99th percentile outputs will sufficiently account for toxicokinetic sensitivities of pregnant women. A statement acknowledging increased uncertainty due to the lack of a fetal compartment has been added to Sections 3.2.6.2 and 4.4.1.
108	**PUBLIC COMMENTS:** EPA acknowledges important pathways – CYP oxidation pathway and GSH conjugation pathway – that are involved in TCE metabolism and lead to the generation of known toxic metabolites including DCA and TCA. EPA further acknowledges variability across the human population with regard to these pathways. • EPA's PBPK model attempts to account for these metabolic differences. However, data gaps introduce uncertainty regarding the extent to which the PBPK model sufficiently addresses these variabilities that make individuals differentially susceptible. EPA should more fully address the extent to which the PBPK model addresses the acknowledged uncertainty and does so in a manner that is health-protective, including specifically for susceptible populations. • EPA states that "[f]or developmental toxicity endpoints, the TCE PBPK model did not incorporate a pregnancy model to estimate the internal dose of TCE in the developing fetus." At a minimum, EPA should explicitly discuss, with supporting evidence, the implications of the absence of a pregnancy model in the PBPK model with regard to deriving PODs and ultimately estimating risk.	

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	• EPA should describe how the protection of vulnerable populations, including the developing fetus, is ensured given EPA's reliance on the existing PBPK model that does not incorporate a pregnancy component.	
94	**PUBLIC COMMENTS:** The kinetic parameters in the PBPK model for the β-lyase enzyme in rats and humans originating from Clewell et al., 2000 have not been documented and pre-date the values that were developed by Green et al. (1997) from *in vitro* studies. The activity of β-lyase in the metabolism of DCVC to the reactive metabolites in the kidney was lower in humans compared to rats.	Additional discussion and citations have been added to Sections 3.2.2.4, 3.2.6.2, and others throughout the document concerning uncertainty around the relative amount of GSH metabolism occurring in rodents compared to humans.
108	**PUBLIC COMMENTS:** EPA should apply an UF of 10 to account for uncertainties for route-to-route extrapolation. The PBPK model used does not account for dermal exposure. EPA's decision to rely on inhalation-to-dermal extrapolation contributes substantial uncertainty to its risk calculations.	Application of oral HED values to dermal exposure is a conservative assumption that is unlikely to underestimate risk. Therefore, an additional UF is not required or appropriate.
62	**PUBLIC COMMENTS:** A population-based PBPK model has been published and showed great similarity in TCE toxicokinetics between humans and mice. The following studies should be reviewed and considered in the assessment as relevant toxicokinetics information: Bradford et al. (2011); Chiu et al. (2014); Yoo et al. (2015a,b,c); and Luo et al. (2018a,b).	EPA's PBPK model is already peer reviewed and was well-supported by the SACC. Therefore, EPA is not making any updates to the model at this time.
34	**PUBLIC COMMENTS:** As heart development appears to be the most sensitive marker of TCE toxicity and Chen et al. (2020) (in the journal "Environmental Science: Processes & Impacts") and other papers have identified a number of appropriate markers in the developing heart (*e.g.,* HNF4a transcription factor), the SACC should recommend that a relative comparison of exposures be obtained by comparing marker expression in the heart and changes in cardiac output between oral and inhalation exposures. At a minimum, this would test the modeling approach used to establish appropriate levels of inhalation exposure.	Almost all mechanistic data on cardiac heart effects were *in vitro* and based on elevated concentrations. Therefore, a direct extrapolation to applied doses/concentrations to exposed human receptors is not possible.
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SACC	**SACC COMMENTS:** Recommendation: Make corrections in statements or provide additional justification about TCE absorption. • Section 3.2, line 537: It was assumed that systemic absorption of inhaled TCE is 100%. Dallas et al. (1991) reported systemic uptake of about 60% of inhaled TCE by rats, with the proportion dependent upon vapor concentration and duration of exposure. Absorption of ingested TCE, in contrast, was relatively complete. More than 90% of TCE given in water by gavage was absorbed by fasted rats (D'Souza et al., 1985). It should be recognized that the majority of low oral doses of TCE are removed from the portal blood by first-pass hepatic and pulmonary elimination, such that very little TCE reaches the arterial circulation (Liu et al., 2009; Mortuza et al., 2018). • Section 3.2, line 549: The assumed percutaneous absorption of 100% is too high. Twenty to thirty percent would be a high estimate. Some Committee members considered the assumption of keeping TCE in contact with the skin under occluded conditions for an extended period as not a realistic exposure scenario. One Committee member pointed out that this might happen if a consumer were using a TCE-containing product without gloves and a product-soaked rag.	EPA has added a statement clarifying that more specific absorption data was incorporated into the PBPK model to 3.2.2.1. Metabolism of TCE including first-pass metabolism is described in Section 3.2.2.3. EPA does not assume 100% dermal absorption except under occluded occupational exposure scenarios, which were not used for risk estimation. As described in Section 3.2.2.1, both occupational and consumer assessments accounted for evaporation in calculating fraction absorbed of TCE under non-occluded (or non-impeded evaporation) conditions. Permeability flux was used in accounting for TCE absorption for consumer scenarios with impeded evaporation.
SACC	**SACC COMMENTS:** Recommendation: The document needs to provide more accurate and complete discussion regarding some key aspects of TCE metabolism and the role of key metabolites in adverse effects caused by TCE. • Section 3.2, lines 595-602, p. 205: Regarding species differences in gamma-glutamyltransferase (GGT) activity, the text is incorrect; mice are higher than humans. See Hinchman and Ballatori (1990) for information on species differences. Total rat and mouse kidney GGT levels are similar. • Section 3.2.3, p. 210-Hazard Identification: Gender- and species-dependent differences, which can be quite prominent, should be mentioned here.	The statement on GGT activity is accurate as written according to Table 3-26 of the IRIS assessment, which cites Lash et al. (1999a; 1998a). Species-specific differences are discussed in Toxicokinetics (Section 3.2.2) and PESS (3.2.5.2) sections. The hazard ID section is purposely kept succinct and full details of all studies are not discussed. A reference to sex-specific differences in GSH conjugation has also

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	• 3.2.3.1.2, p. 211-Kidney Toxicity, lines 779-780: The text states: "this toxicity is likely caused by DCVC formation, with possible roles for TCOH and TCA…" There are no data supporting a role for TCOH or TCA in kidney toxicity.	been added to PESS section 3.2.5.2. EPA deleted "with possible roles for TCOH and TCA."
SACC	**SACC COMMENTS:** Recommendation: The document should cite recent reviews of TCE metabolism that have appeared after release of the EPA TCE IRIS assessment in 2011. • See Lash et al. (2014), Cichocki et al. (2016), and Luo et al. (2018) for comprehensive reviews of TCE toxicokinetics and mechanisms of toxicity and carcinogenicity.	These have been added where relevant to the toxicokinetics section in 3.2.2. (Cichocki et al. 2016) was also cited in the PESS section, while the (Cichocki et al. 2016) and several Lash studies were incorporated into the MOA (3.2.4.2.2) and Metabolism (3.2.2.3) sections.
SACC	**SACC COMMENTS:** The committee commented on the written and oral comments from Dr. James Bus (Commenter 63) at the public meeting focusing primarily on a new study he co-authored (Zhang et al., 2018) on the relevance of the glutathione-dependent metabolism pathway for TCE and its role in TCE induced kidney toxicity and kidney cancer. • Generally, the committee viewed the key points raised by Dr. Bus to be un-substantiated and long resolved, and the point of the comments unclear since dismissing the kidney as a target organ for TCE would have no impact on the TSCA hazard assessment for TCE.	EPA agrees with the SACC and the results of Zhang et al, 2018 (available at https://www.sciencedirect.com/science/article/pii/S0378427418314905) were not incorporated into the risk evaluation.
63, 94	**PUBLIC COMMENTS:** The non-specific HPLC spectrophotometric method used in several studies that report levels of DCVG has a substantial potential for chromatographic overlap with peaks of endogenous metabolites that can result in an overestimation. This was shown in Zhang et al. (2018) using a side-by-side comparison of a TCE metabolite-specific HPLC MS/MS method, and indicates that DCVG concentrations reported in the earlier literature are not reliable for modeling human kidney cancer. A structure-specific HPLC electrospray ionization (ESI)-MS/MS method is also available. None of the data using these updated approaches were incorporated in the draft.	
62	**PUBLIC COMMENTS:**	

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	The toxicokinetics section, based on EPA (2011e), is incomplete. Data are now available on organ-, sex-, and strain-specific metabolism of TCE (gavage) through both oxidative and conjugation pathways. These studies provide strong evidence that GSH conjugation metabolites are produced *in vivo* upon exposure to TCE and reveal organ-specific information on the levels of these mutagenic species. Information on inter-organ pathways for metabolism of TCE by the GSH conjugation pathway is provided in the reviews by Lash et al. (2014; PMID: 25484616 PMCID: PMC4254735) and Rusyn et al. (2014; PMID: 23973663 PMCID: PMC3867557). These reviews cite other relevant studies.	EPA has added additional detail to the toxicokinetics and PBPK modeling sections under Section 3.2.2.
Liver and kidney toxicity		
SACC	**SACC COMMENTS:** Recommendation: Modify overstatements in Section 3.2.3.1.1 and 3.2.4.1.3. • The Committee felt that several statements are too broad or overstate the case for liver or kidney toxicity. These include: Section 3.2.3.1.1 p. 210, line 713 that "Animals and humans exposed to TCE consistently experience liver toxicity," and lines 729-730 "Several human studies…reported an association between TCE exposure and significant changes in serum liver function tests… ," and Section 3.2.4.1.3, p. 220, line 1180 "Both animal and human studies consistently observe induction of kidney toxicity…and progression of existing kidney disease." It was noted that serum enzyme changes indicative of liver toxicity in rodents occurred at high doses and that hepatotoxicity was rarely reported in patients for whom it was used as an anesthetic. It was also noted that nephrotoxicity has not been consistently observed in occupational exposure studies, and that evidence of renal proximal tubular damage is usually mild and limited to increases in certain cytoplasmic enzymes in urine, and that such effects typically require chronic TCE exposures.	EPA has modified statements indicating that studies "consistently" show liver or kidney toxicity. The statements indicating that multiple studies demonstrate toxicity are true however and those have not been modified.
SACC	**SACC COMMENTS:**	

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	Recommendation: Clarify what information from Kjellstrand et al. (1983) is used to calculate the POD for liver toxicity. It is not clear what inhaled concentration examined in the study by Kjellstrand et al. (1983) was used in the draft risk evaluation to calculate the POD. It is difficult to tell from the publication what the NOAEL and/or LOAEL are for increased liver weight. It appears that 75 ppm was the LOAEL for liver weight, but 150 ppm was required to cause cytoplasmic vacuolization. It is not clear whether the vacuolization was due to lipid, glycogen or water accumulation. Any of these could contribute to increased liver weight, which is said in line 2115 to be "merely adaptive," as opposed to cytotoxic. The quality of the Kjellstrand data needs to be better assessed and more discussion provided as to whether the observed effect was adverse or adaptive.	Clarification has been added that vacuolization and inflammatory infiltration occurred at 150ppm and above, and increased liver weight occurred at ALL dose groups and durations Inflammatory cell infiltrates would definitely be considered adverse, and likely are related to immunotoxicity effects since hepatitis is often observed as an outcome of hypersensitivity responses.
SACC	**SACC COMMENTS:** There was concern regarding the evaluation of liver toxicity. The Woolhiser et al. study was excluded because increased liver weight was not accompanied by other indications of toxicity despite an almost identical $BMLD_{10}$ value in the Kjellstrand et al. study. The conclusion that the increased liver weight observed in Woolhiser et al. is an adaptive response rather than an indicator of toxicity seems speculative and needs better support.	Liver weight changes alone without any other indications of toxicity is considered adaptive. Both (Buben and O'Flaherty, 1985) and (Kjellstrand et al., 1983) demonstrated other liver effects, but (Woolhiser et al., 2006)only showed liver weight increases.
SACC	**SACC COMMENTS:** Recommendation: Address the utility/limitation of using the rat data of Maltoni et al. (1986) to extrapolate to human kidney risk, in view of the substantially greater metabolic activation of TCE via the GSH pathway in rats than in humans. • The Committee expressed concern with the use of the rat data of Maltoni et al. (1986) to establish the POD for nephrotoxicity, considering the relatively high metabolic activation of TCE in rats, as demonstrated by Green et al. (1997a,b), Bernauer et al. (1996), Cooper (1994), and Lash et al. (1990, 2014). It was also noted that Lash (2001) demonstrated that cultured rat renal cells were more sensitive to DCVC than human renal cells.	This comment is not specific to the study and merely expresses uncertainty about extrapolation of rat kidney data to humans in general. These differences should be accounted for in the PBPK model, although uncertainties about GSH conjugation parameters in the model are acknowledged in 3.2.6.2. (Bernauer et al. 1996) actually concluded that you cannot compare the data between rats and humans, only that they both do use the pathway. The following text has been added to the section:

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		"There is additional uncertainty in extrapolation to humans based on evidence suggesting that metabolic formation of the reactive conjugative metabolites may be an order of magnitude greater in rats than humans (Green et al. 1997b; Lash et al. 1990) and that renal toxicity may not be directly related to the rate of DCVC formation (Green et al. 1997a, b). These metabolites are indeed formed in both rats and humans, however, (Bernauer et al. 1996) and *in vitro* data suggests that human GSH conjugation activity may actually be higher than rodents in some cases (Table 3-23 and 3-26 of (U.S. EPA, 2011e)). Additionally, their slow elimination kinetics relative to oxidative species indicate that even lower relative concentrations may contribute to sustained chronic toxicity (Bernauer et al. 1996)."
108	**PUBLIC COMMENTS:** EPA dismisses an NTP study of kidney toxicity without sufficient justification. • EPA selects Maltoni et al. (1986) as the representative study for the kidney toxicity endpoint, a departure from the 2014 Work Plan Assessment, in which the NTP (1988) study was selected because it provided the lowest POD. • Both studies were rated as "medium" quality, and the HEC99 for Maltoni et al. (1986) is nearly 5 times higher. • EPA justifies the decision stating "elevated doses in the NTP study resulted in massive nephrotoxicity and introduce large uncertainty in BMD modeling the effects at low doses well below the tested doses with a BMR well below the observed effect incidence in the study;" this issue was directly addressed in the 2011 IRIS assessment and deemed not to represent a concern to warrant not relying on the NTP	Consideration of dose levels in a study compared to the extrapolated BMDL is discussed in EPA's *Benchmark Dose Technical Guidance Document* (U.S. EPA, 2012a). The (NTP, 1988) study itself includes a statement at the beginning indicating that the doses were recognized as too high for sensitive evaluation of effects.

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	study. Given that (1) the NTP study provides the *lowest* HEC99 on the *most severe* kidney toxicity endpoint and (2) modeling challenges did not present concerns in prior assessments, EPA should select the POD from the NTP 1988 study rather than the Maltoni et al. (1986) study to represent the kidney toxicity endpoint.	
62	**PUBLIC COMMENTS:** EPA stated that it did not identify any new repeat-dose experimental studies in animals or human epidemiological studies that would contribute significant additional hazard information for kidney toxicity. However, there are additional informative studies. For example, a study by Yoo et al. (2015; HERO ID 2799570; PMID: 25424545; PMCID: PMC4281933) examined TCE metabolite levels and toxicity phenotypes in kidneys in mice of various strains after subacute and subchronic exposures. Data from the subchronic experiment should be extracted for dose-response analysis.	This study is primarily examining toxicokinetics in kidney and does not include any novel endpoints or dose-response information.
62	**PUBLIC COMMENTS:** Tables 22-24 in the Data Quality Evaluation document provide results of the review of the study quality of two companion studies by Yoo et al. (2015) [HERO IDs 2799569 and 2799570]. These studies report data for liver and kidney effects in two separate manuscripts; however, the data were collected in the same set of *in vivo* studies and the same strengths and weaknesses should apply. The document included separate evaluations of the subacute and subchronic experiments for liver endpoints, but not kidney endpoints. It is recommended that for consistency, the data on renal outcomes should be evaluated separately between subacute and subchronic study arms, as was done for the liver.	This will be taken into account for consideration in future Risk Evaluations.
Developmental toxicity (other than fetal cardiovascular defects)		
SACC	**SACC COMMENTS:** One Committee member indicated that the draft risk evaluation (and the TSCA program in general) need to define the term "developmental toxicity." It is not clear whether this refers to toxicity that is induced by developmental exposure, but which may manifest at any time during life,	Developmental toxicity refers to endpoints affecting fetal or neonatal outcomes. This definition has been added to Section 3.2.3.1.6.

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	or refer only to pathologies that occur during infancy and childhood.	
SACC	**SACC COMMENTS:** Recommendation: Justify why developmental toxicity was not given more consideration in the risk characterization. • There is evidence from both epidemiological and animal studies that developmental toxicity may be an especially sensitive endpoint for TCE. The draft risk evaluation discounts investigations describing these effects, because some did not demonstrate dose-dependency, some were mouse strain-specific, or some were not of adequate quality. Studies from Camp Lejeune indicate adverse developmental effects may occur in response to TCE exposures lower than those required to cause toxicity in adults. Assessment of this endpoint is especially important. The study by Peden-Adams et al. (2006) exhibited one of the lowest PODs among developmental toxicity studies but was scored Low and not considered for risk characterization. This was considered unacceptable by at least one Committee member, who noted that other immunotoxicity studies of inferior quality received higher quality ratings and were considered key studies.	Developmental toxicity is thoroughly considered in the risk evaluation, and three developmental endpoints are included for risk estimation. While (Peden-Adams et al., 2006) did receive a Low rating, EPA notes in the document that the POD from (Keil et al., 2009) is almost identical to the (Peden-Adams et al., 2006) POD and would therefore be expected to be protective of those developmental effects.
SACC	**SACC COMMENTS:** Recommendation: Clarifications and corrections are needed. Section 3.2.3.1.6, pp. 215-216: The draft risk evaluation states (lines 950-952) that aside from congenital heart defects, it does not identify any repeat-dose experimental studies in animals or human epidemiological studies that would contribute significant additional information for developmental effects. Then the draft risk evaluation goes on to describe numerous papers (including studies from Camp Lejeune exposure) that associate developmental TCE exposure to various developmental outcomes in humans such as spontaneous abortion, developmental neurotoxicity, and childhood cancers. This is very confusing and needs to be clarified.	EPA has clarified that the statement applies to "new" studies, as in studies published after previous EPA assessments (*e.g.,* IRIS Assessment, 2014 Risk Assessment).
SACC	**SACC COMMENTS:** Recommendation: Describe and discuss the findings of recent	An endpoint for developmental neurotoxicity

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	investigations of adverse effects of TCE on the developing nervous system. EPA adequately addresses acute neurotoxic effects such as CNS depression, but should consider recent investigations of developmental neurotoxicity (Salama et al., 2018; Blossom et al., 2017).	from (Fredriksson et al., 1993) is included as a representative POD for developmental toxicity and risk estimation. EPA has also added hazard information from (Blossom et al. 2016) (correct citation for Blossom et al., 2017) and (Salama et al. 2018) as recommended to Section 3.2.3.1.6.
100	**PUBLIC COMMENTS:** EPA ignores evidence of TCE's developmental effects. • In its 2014 risk assessment of TCE's degreasing, spot cleaning and arts and crafts uses, EPA wrote "the available studies collectively suggest that the developing brain is susceptible to TCE toxicity…studies have reported an association with TCE exposure and CNS birth defects and postnatal effects such as delayed newborn reflexes, impaired learning or memory, aggressive behavior, hearing impairment, speech impairment, encephalopathy, impaired executive and motor function and attention deficit." Since 2014, several additional studies have reported further evidence of TCE's neurodevelopmental effects. However, EPA fails to consider those more recent studies in its evaluation, and therefore, fails to adequately evaluate the neurodevelopmental risk of exposure throughout pregnancy, a likely scenario for pregnant workers.	
105, 108	**PUBLIC COMMENTS:** The study by Peden-Adams et al. (2006) provides a sensitive developmental toxicity endpoint for the dose-response assessment of TCE. The IRIS toxicology review of TCE used Peden-Adams et al. (2006) to support the derivation of the TCE RfD, indicating that "[f]or adult and developmental immunological effects, there is high confidence in the evidence of immunotoxic hazard from TCE." Yet, for the draft risk evaluation, Peden-Adams et al. (2006) was excluded by EPA in its dose-response assessment and a POD was not derived. EPA explained "while this endpoint exhibits one of the lower PODs among developmental studies, the study scored a "Low" in EPA's data quality evaluation due	While (Peden-Adams et al., 2006) did receive a Low rating, EPA notes in the final risk evaluation that the POD from (Keil et al., 2009) is almost identical and would therefore be expected to be protective of those developmental effects. EPA often uses expert judgement to downgrade or upgrade studies from the calculated scores when the metrics do not sufficiently account for all considerations of data quality. The evaluation for this study was

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	to concerns over statistical reliability and dose precision." • However, the systematic review evaluation resulted in a score of "Medium" quality. The "Medium" rating appears crossed out (*i.e.,* strikethrough text) and changed to "Low." The footnote provides, as the rationale for the rating change, the same criteria that supported the "Medium" quality rating. This study should receive the same "Medium" rating consistently throughout the document. The conclusions of study quality should be scrutinized due to a problematic systematic review method. EPA also stated that this study could not be accurately PBPK modeled because exposure occurred in utero, through nursing, and after weaning. • The fact that the PBPK model cannot accommodate the exposure scenario in the Peden-Adams et al. (2006) study is an issue with the model, not a flaw in the study. • The earlier EPA IRIS analysis for the RfD (U.S. EPA, 2011) was able to calculate doses for the Peden-Adams et al. (2006) study, based on information from the authors. That analysis calculated a LOAEL of 0.37 mg/kg-day (1.4 ppm) TCE. This study should not have been excluded due to the erroneous "Low" rating or because the data could not be used in an existing PBPK model.	reviewed several times by EPA subject matter experts who agreed with the final score.
89	**PUBLIC COMMENTS:** Links between TCE and specific cancers and to birth defects must be taken more seriously. The following studies suggest a strong link between exposure to low levels of TCE and certain cancers and developmental effects: Chiu et al. (2013); Forand et al. (2012); Caldwell et al. (2008); Drake et al. (2006); and Peden-Adams et al. (2007).	These studies were all included in the draft Risk Evaluation and have been retained in the final version. Multiple endpoints for developmental toxicity and cancer at multiple tumor sites were included in risk estimation.
Other endpoints		
SACC	**SACC COMMENT** Recommendation: Clarifications and corrections are needed. • Section 3.2.3.1.4, p. 212: In discussing TCE-induced neurotoxicity in humans, the document needs to make it clear that TCE exposures for neurological effects are generally at quite high doses. • At least one Committee member considered the statement in Section	The commenter must mean Section 3.2.3.1.3. EPA disagrees that neurotoxicity effects are only at high doses, as PODs for the key neurotoxicity endpoints are all based on LOAELs ranging from 12-47 mg/kg-day.

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	3.2.4.1.5 p. 220, lines 1212-1214 to be inaccurate. The declaration that there is strong evidence from human and animal data of male reproductive effects is, in their opinion, overstated. The statement about insufficient evidence for TCE-induced female reproductive toxicity is incorrect. • Section 3.2.3.1.5 – Reproductive toxicity, p. 214: Six studies published in 2016, 2018, 2019, and 2020 by R. Loch-Caruso and colleagues that provide evidence of female reproductive toxicity of TCE *in vivo* and DCVC *in vitro* are not identified or discussed. See Hassan et al. (2016); Elkin et al. (2018); Elkin et al. (2019); Hassan et al. (2019); and Elkin et al. (2020).	"Strong" has been changed to "consistent," since multiple epidemiological and animal studies have observed male reproductive effects. The 2020 Elkin review (Elkin et al. 2020) and the cited 2019 animal study ((Loch-Caruso et al. 2019), cited here as Hassan 2019) have been cited in the hazard ID section, 3.2.3.1.5, however it is noted that the significance of DCVC to reproductive tox is unclear.
108	**PUBLIC COMMENTS:** SACC members raised additional concerns around the absence of studies on specific topic areas. One panelist noted the absence of sufficient information on female reproductive toxicity. Another indicated that TCE-induced occupational dermatitis is prevalent but that much of the relevant literature is published in a foreign language. EPA should include relevant studies published in languages other than English when pertinent to a risk evaluation and employ necessary resources to have them translated to ensure these studies are captured.	The 2016 study was identified in the literature search but did not pass PECO because except for cardiac malformations or other developmental toxicity outcomes, mechanistic studies (especially on metabolites) were excluded. The other studies were all published after the lit search cutoff date in 2017. In the WOE section (3.2.4.1.5), the WOE for female reproductive effects was also upgraded from “insufficient information” to “limited information” supporting the outcome. Foreign language studies are outside the scope of EPA’s PECO statements as published in the Problem Formulation document.
60	**PUBLIC COMMENTS:** For endpoints other than fetal cardiac defects, the rationale for selection of studies for use in risk evaluation from those available was not transparent.	Section 3.2.5.1 in the Risk Evaluation lists the acceptable studies containing adequate dose-response information. Among those studies, detailed considerations for the studies and PODs

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		selected among that group are provided in Section 3.2.5.3.
81	**PUBLIC COMMENTS:** Is TCE linked with Parkinson's disease, and if yes, how can we decelerate the disease and prevent the manifestation of clinical symptoms?	This comment is beyond the scope of the TCE Risk Evaluation.
General		
SACC	**SACC COMMENT** Recommendation: Make sure that broad terminology that may be unclear to some readers is defined. • Section 3.2, lines 487-488, p. 202: What exactly does "acute overt toxicity" mean? This is an odd term that needs to be explained.	The term has now been defined in the section (3.2.3.1.7).
SACC	**SACC COMMENT** Recommendation: Clarifications and corrections are needed. • Section 3.2.5.2, p. 233, lines 1822-1862: NRC (2009) reviewed factors influencing susceptibility of human populations to TCE toxicity and carcinogenicity. This comprehensive review might be cited here.	EPA has added a reference to the NRC assessment, which was actually in 2006 (NRC, 2006).
91	**PUBLIC COMMENTS:** Current research shows that TCE is linked to liver cancer, kidney cancer, Parkinson's Disease, congenital heart defects, and other diseases. EPA has not adequately evaluated available data and is not justified in taking this action. Please conduct a thorough review of the existing literature and reevaluate. A reliable risk evaluation of TCE cannot be made using a fraction of the relevant scientific information.	EPA has performed a thorough systematic review on the reasonably available literature for TCE as of February 2017. EPA does not believe that it missed any relevant studies and has identified each of the health effects mentioned in the comment within the Risk Evaluation. Additionally, EPA has added select relevant individual studies identified to EPA that were published after that date (Harris et al., 2018; Charles River Laboratories, 2019).
32	**PUBLIC COMMENTS:** There has been no federal support for the investigation of TCE and congenital heart defects since 2009 and a recommendation in this area by the SACC could be useful.	EPA always encourages additional research that may yield more useful information.

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32	**PUBLIC COMMENTS:** Despite the substantial data referenced in the draft document showing that TCE produces congenital heart defects, the draft recommendations do not reference this issue in any affected population. I would argue that any and all uses of TCE, as described in the draft, should be accompanied by an explicit warning that low levels of TCE can cause heart defects and that women who are pregnant or who might be pregnant should avoid any and all exposure to the solvent.	Per the statute (see TSCA section 6(b)(4)(A)) and the implementing regulations for risk evaluations (40 CFR part 702, subpart B), during risk evaluation, EPA must determine whether the chemical substance presents unreasonable risk under its conditions of use. Upon finding unreasonable risk, EPA will apply risk management actions to the extent necessary so that the chemical no longer presents such risk, in accordance with TSCA section 6(a). Warning labels are one of the regulatory management components that EPA considers during risk management.
45	**PUBLIC COMMENTS:** The following relevant studies were not included in the draft risk evaluation: • Alterations in immune and renal biomarkers among workers occupationally exposed to low levels of trichloroethylene below current regulatory standards. Lee KM, Zhang L, Vermeulen R, Hu W, Bassig BA, Wong JJ, Qiu C, Purdue M, Wen C, Walker DI, Jones DP, Li L, Huang Y, Rothman N, Smith MT, Lan Q. Occup Environ Med. 2019 Jun;76(6):376-381. doi: 10.1136/oemed-2018-105583. Epub 2019 Apr 10. • Trichloroethylene perturbs HNF4a expression and activity in the developing chick heart. Harris AP, Ismail KA, Nunez M, Martopullo I, Lencinas A, Selmin OI, Runyan RB. Toxicol Lett. 2018 Mar 15;285:113-120. doi: 10.1016/j.toxlet.2017.12.027. Epub 2018 Jan 4. • [Role of complement regulatory protein CD55 in the liver immune injury of trichloroethylene-sensitized mice]. Wang X, Zhang C, Yang XD, Li BD, Zang DD, Yang P, Zhang JX, Zhu QX. Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi. 2017 Apr 20;35(4):246-250.	The 2019 study was published after the conclusion of EPA's literature search and would not add any significant new information to hazard conclusions since kidney toxicity was already included in risk estimations. (Harris et al., 2018) was included in the cardiac defects WOE analysis. (Gilbert et al., 2017) was included in the on topic literature but not cited in the RE because it did not include any significant information beyond what was already discussed. EPA did add discussion of (Gilbert et al. 2014) covering developmental immunotoxicity. (Meadows et al., 2017) was not included in the literature search and was not cited for the same reason as above. Jiang et al. 2017 (actually (Jiang et al., 2016)) also was outside the window of the literature search and

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	doi: 10.3760/cma.j.issn.1001-9391.2017.04.002. Chinese. • Exposure cessation during adulthood did not prevent immunotoxicity caused by developmental exposure to low-level trichloroethylene in drinking water. Gilbert KM, Bai S, Barnette D, Blossom SJ. Toxicol Sci. 2017 Jun 1;157(2):429-437. doi: 10.1093/toxsci/kfx061. • A single dose of trichloroethylene given during development does not substantially alter markers of neuroinflammation in brains of adult mice. Meadows JR, Parker C, Gilbert KM, Blossom SJ, DeWitt JC. J Immunotoxicol. 2017 Dec;14(1):95-102. doi: 10.1080/1547691X.2017.1305021. • The role of miR-182-5p in hepatocarcinogenesis of trichloroethylene in mice. Jiang Y, Chen J, Yue C, Zhang H, Tong J, Li J, Chen T. Toxicol Sci. 2017 Mar 1;156(1):208-216. doi: 10.1093/toxsci/kfw246.	did not add significant novel information that would affect the conclusions of the Risk Evaluation.

6. Risk Characterization

Risk Characterization		
Charge Question 6.1: Please comment on whether the information presented to the committee supports the conclusions outlined in the draft risk characterization section concerning TCE. If not, please suggest alternative approaches or information that could be used to further develop risk estimates within the context of the requirements stated in EPA's Final Rule, *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* (82 FR 33726) (Section 4). **Charge Question 6.2:** EPA presented overall human health risk conclusions (Section 4.5.2) based on risk estimates for the endpoints that it believes are best representative of acute and/or chronic scenarios (see Question 5.3 - immunosuppression for acute exposure, autoimmunity for chronic exposure). Please comment on EPA's approach including any alternative considerations for determining and presenting risk conclusions including the risk summary tables (Table 4-54 and 4-55). **Charge Question 6.3:** Please comment on the calculation of risk derived from different exposure data sources (*e.g.,* modeling tools and monitored datasets) and how they account for variability in environmental and human exposure. Please provide specific recommendations as needed for improving the risk characterization and references to support any recommendations (Section 4). **Charge Question 6.4:** Please comment on whether the risk evaluation document has adequately described the uncertainties and data limitations associated with the methodologies used to assess the environmental and human health risks. Please comment on whether this information is presented in a clear and transparent manner (Section 4.3). **Charge Question 6.5:** Please comment on the clarity and validity of specific confidence summaries presented in Section 4.3. **Charge Question 6.6:** Has a thorough and transparent review of the available information been conducted that has led to the identification and characterization of all PESS (Sections 2.3.3, 3.2.5.2, and 4.4.1)? Do you know of additional information about PESS that EPA needs to consider? Additionally, has the uncertainty around PESS been adequately characterized? **Charge Question 6.7:** Please comment on whether EPA has adequately, clearly, and appropriately presented the reasoning, approach, assumptions, and uncertainties for characterizing risk to workers and ONUs using PPE (exposure - Sections 2.3.1.2.6 and 2.3.1.3, Table 2-20; risk - Sections 4.2.2 and 4.3.2.1). **Charge Question 6.8:** Please comment on any other aspect of the environmental or human health risk characterization that has not been mentioned above (Section 4).		
#	**Summary of Comments for Specific Issues Related to Charge Question 6**	**EPA/OPPT Response**
Cancer risk benchmark is not valid		
56, 108	**PUBLIC COMMENTS:** EPA's unprecedented use of 1 in 10,000 as the cancer risk benchmark for workers underestimates risk and violates EPA's long-standing policy "that it should reduce risks to less than 1 x 10^{-6} for as many exposed people as reasonably possible." Workers are specifically	As noted in the draft risk evaluation, EPA relied on Agency precedent and NIOSH guidance when choosing the 10^{-4} cancer risk benchmark to evaluate risks to workers from TCE exposure.

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	identified under TSCA as a vulnerable subpopulation warranting special protection.	The standard cancer benchmarks used by EPA and other regulatory agencies range from 1 in 1,000,000 to 1 in 10,000 (*i.e.,* $1x10^{-6}$ to $1x10^{-4}$) depending on the subpopulation exposed. Generally, EPA considers $1x10^{-6}$ to $1x10^{-4}$ as the appropriate benchmark for the general population, consumer users, and non-occupational PESS. EPA, consistent with 2017 NIOSH guidance, used $1x10^{-4}$ as the benchmark for the purposes of this unreasonable risk determination for individuals in industrial and commercial work environments, including workers and ONUs. EPA has consistently applied a cancer risk benchmark of $1x10^{-4}$ for assessment of occupational scenarios under TSCA. $1x10^{-4}$ is not a bright line and EPA has discretion to make unreasonable risk determinations based on other benchmarks as appropriate. See Section 5.1.1.2 of the risk evaluation for additional information.
56, 69, 108	**PUBLIC COMMENTS:** EPA's use of a 1 in 10,000 cancer risk level as reasonable is flawed. EPA cites this benchmark for workers to NIOSH (under OSHA) and the Benzene decision despite indicating that TSCA has different standards. • There is no basis in TSCA (including 2016 amendments) for EPA to provide less protection to workers than to any other potentially exposed or susceptible subpopulation. • EPA's reliance on the Benzene decision is unfounded because EPA cannot point to statutory language in TSCA evoking the same standard to regulate significant risks (under the Occupational Safety and Health Act) rather than unreasonable risks (under TSCA). • In implementing TSCA, EPA has generally sought to reduce population risks from chemicals in commerce that are carcinogens to one case per million people (*i.e.,* $1x10^{-6}$ risk level). • EPA mentions uses of a $1x10^{-4}$ risk level based on the "two-step approach" under the CAA; however, that level reflects the limit on maximum individual lifetime cancer risk (rather than a level set to protect the vast majority of the population). EPA erroneously invokes the risk level $1x10^{-4}$ to numerous COUs so that no risk is identified for workers, subjecting workers to cancer risks that are two orders of magnitude higher than warranted. This approach must be rejected on scientific and legal grounds.	
56, 69, 74, 108	**PUBLIC COMMENTS:** EPA's use of a $1x10^{-4}$ risk level failed to identify risk as unreasonable in numerous cases and understates the magnitude of the cancer risk even where it is identified as unreasonable. • Using a benchmark of $1x10^{-5}$ or $1x10^{-6}$, unreasonable cancer risk would have been identified in 11 or 12 additional cases (identified in 79 of 91 cases using $1x10^{-4}$). • Where unreasonable risk was identified, use of the appropriate benchmark would have established the need to reduce exposure by	

	10-fold via TCE regulations to eliminate unreasonable risk.	
74	**PUBLIC COMMENTS:** EPA applied a cancer risk benchmark up to two orders of magnitude less protective than warranted. EPA's benchmark of 1 in 10,000 means that it provides far less protection to workers than the general population, let alone other vulnerable subpopulations, directly contravening TSCA. The only support that EPA cites is policy and practice under other laws or by other agencies, ignoring the fact that their standards differ fundamentally from that of TSCA.	
99	**PUBLIC COMMENTS:** EPA used a cancer risk of $1x10^{-4}$ as the benchmark for determining unreasonable risk to workers. This benchmark results in a significantly smaller number of worker exposure scenarios that present unreasonable risks than under cancer risk levels of $1x10^{-5}$ and $1x10^{-6}$. The SACC has stated that EPA has not provided "adequate explanation and justification" for this reduced threshold and that the TCE draft risk evaluation fails to justify EPA's approach. Despite reserving discretion to make case-by-case decisions within the range, however, EPA has identified $1x10^{-6}$ as its goal for public health protection. However, EPA's recent draft risk evaluations deviate from this approach for worker exposures, maintaining that risks smaller than $1x10^{-4}$ will be considered "reasonable" under TSCA because, "consistent with case law and 2017 NIOSH guidance," this risk level applies to "industrial and commercial work environments subject to Occupational Safety and Health Act (OSHA) requirements." However, the Occupational Safety and Health Act precedent does not control decision-making under TSCA, a separate law with different purposes and wording. • The cancer risk threshold applied by NIOSH and OSHA is rooted in the Benzene decision and is based on the finding that significant risks are present. • TSCA is anchored in the concept of "unreasonable risk" (a lower risk threshold than "significant risk"); no provision of TSCA provides that workers should receive less protection than other	

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	exposed populations or that well-established benchmarks for unacceptable cancer risks would be inapplicable to workers. • TSCA protects workers from exposures in the workplace as well as from other sources, such as environmental releases and consumer products. Since the draft risk evaluation assesses worker exposures in isolation from other pathways, risks are already understated. EPA must apply to workers the same benchmarks for determining unreasonable cancer risk that it uses for other populations. For all populations, EPA should consider increased cancer risk exceeding $1x10^{-6}$ to be unreasonable and to require action under TSCA.	
100	**PUBLIC COMMENTS:** When measuring cancer risks for non-workers potentially exposed or susceptible to a chemical, EPA considers a range of one increased incidence of cancer in every 10,000 to 1,000,000 people as evidence of unreasonable risk. For workers, however, EPA uses only the lowest end of the range, characterizing increased cancer risks of up to 1 in 10,000 workers as reasonable and not warranting regulation. Although EPA cites NIOSH for this benchmark, NIOSH is not required to set risk management limits at levels that avoid unreasonable risk to PESS. EPA also cites AFL-CIO v. American Petroleum Institute 448 U.S. 607 (the "Benzene decision") to support its decision, even though it has no bearing on EPA's duty to identify and manage unreasonable risks under TSCA. Consistent with NIOSH recommendations, EPA should reduce exposure to occupational carcinogens as much as possible, the extent of which should be decided during risk management, and not risk evaluation. When TSCA was amended in 2016, a requirement was added that risk evaluations analyze risks to PESS including workers. Despite this mandate, EPA's draft risk evaluation accepts greater risks to workers than the general population. Whereas 1 in 10,000 to 1,000,000 was used as a measure of unreasonable cancer risk for non-workers potentially exposed or susceptible, EPA uses the lowest range for workers,	

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	characterizing risks of up to 1 in 10,000 as reasonable and not warranting regulation. There is not valid reason to accept such high risks to workers.	
Cancer risk estimates should be calculated for acute exposure		
56, 108	**PUBLIC COMMENTS:** EPA failed to include estimates of acute cancer risk to workers and consumers. • EPA states that the "extrapolation of lifetime theoretical excess cancer risks to single exposures has great uncertainties" and that "the relationship between a single short-term exposure to TCE and the induction of cancer in humans has not been established in the current scientific literature." • NRC guidance recommends applying the linearized multistage model to assessing carcinogenic risks based on exposures of short duration, and that the decision to conduct such extrapolation and modeling should be based on the "sound biological and statistical principles." • There is concern that EPA did not sufficiently consider such principles related to MOA in deciding not to model acute cancer risk. In particular, given that: (1) EPA recognizes that "there is sufficient evidence that TCE-induced kidney cancer operates primarily through a mutagenic mode of action" and (2) a mutagenic MOA suggests a role for "a single direct reaction, specifically, a single hit in a single target," a linear low-dose extrapolation from chronic to acute exposures would be the appropriate approach to take for TCE. EPA's current approach assumes that acute exposures to TCE, including to consumers, pose zero cancer risk – an assumption not warranted based on the WOE. EPA needs to apply an extrapolation that provides a scientifically sound estimate for cancer risk from acute and short-term exposures to TCE.	*Standard Operating Procedures for Developing Acute Exposure Guideline Levels for Hazardous Chemicals* notes the significant uncertainty in extrapolating risks from lifetime exposures to shorter (once in a lifetime) exposures. The SOP specifically points out the complex nature of biological mechanisms related to cancer and possible differences in such mechanisms when considering them for acute vs. chronic exposures. Krewski et al. (2004) further notes that there are often limited single-exposure inhalation toxicity data to consider such an extrapolation from lifetime exposures. For these reasons, EPA doesn't consider use of short-term cancer risk estimates to be appropriate for the current risk evaluation.
99	**PUBLIC COMMENTS:** It is recognized that genotoxic carcinogens like TCE can induce cancer	

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	following a limited acute exposure event and methods are available to estimate such risks. As stated in the 2011 NRC report, there is methodology for extrapolating findings of carcinogenicity in long-term studies to exposures of short duration. EPA acknowledges the possibility of calculating acute cancer risks in the draft risk evaluation but declines to do so owing to "uncertainties" in the methodology. Rather than dismissing acute cancer risks because they are harder to estimate, EPA should have quantified these risks using the framework outlined by NRC, which reflects the best available science.	
Use of unified linear risk approach instead of MOE approach		
56, 108	**PUBLIC COMMENTS:** In accordance with the NAS report (Science and Decisions: Advancing Risk Assessment), EPA must employ health-protective approaches to dose-response modeling, including the recommendation that cancer and non-cancer responses be assumed linear as a default. The MOE approach provided in the draft risk evaluation fails to provide a measure of population risk at a given exposure level, which limits its utility for risk managers. • The NAS Committee on Improving Risk Analysis Approaches concluded that separation of cancer and non-cancer outcomes in dose-response analysis is artificial, because non-cancer endpoints can occur without a threshold or low-dose nonlinearity at the population level; background exposures and underlying disease can contribute to background risk and lead to linearity at population doses of concern. EPA should implement the recommendation by NAS to develop a unified approach to presenting dose-specific population risks for cancer and non-cancer endpoints.	EPA relied on existing accepted guidance (*e.g.,* (EPA, 2012a, 2005a, 2002)) to evaluate noncancer and cancer endpoints in the current risk evaluation of trichloroethylene. These methods include PBPK models for TCE-specific distributional information on toxicokinetics among rodents and humans; appropriate uncertainty factors for non-cancer endpoints; and a linear low-dose extrapolation to model risk from cancer, based on a likely genotoxic MOA. EPA believes that these methods adequately account for variability and susceptibility within the population, a concern raised by NRC (2009). However, EPA will investigate additional scientific approaches for our next set of TSCA risk evaluations.
99	**PUBLIC COMMENTS:** The draft risk evaluation, building on previous determinations, concluded that TCE is genotoxic and uses linear extrapolation. However, at the SACC meeting, some industry presenters urged that EPA base cancer risks on a non-linear MOA. We strongly recommend	EPA used a linear no-threshold model for calculating cancer dose-response. The SACC agreed with the use of a linear model based on the MOA and EPA Guidelines for Carcinogen

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	against this approach. EPA's Guidelines for Carcinogen Risk Assessment emphasizes that a high level of evidence is necessary to deviate from the presumption of linearity.	Risk Assessment.
Description of uncertainties and data limitations in Section 4.3 is incomplete		
SACC	**SACC COMMENTS:** Recommendation: Clarify how the results of exposure uncertainty analysis are used in the characterization of consumer risk, and consider performing a more comprehensive uncertainty analysis (*i.e.,* varying parameters instead of using defaults, for example). The Committee was unclear about how the results of the limited (*i.e.,* only some inputs were varied) uncertainty analysis for consumer exposure were incorporated into the risk characterization and why a more comprehensive uncertainty analysis was not performed.	EPA varied key parameters governing the known product range of weight fractions and user behavior (mass and duration) in order to present a range of potential exposures (referred to as "user intensity levels") in the RE. Risk estimates were presented at low, medium, and high user intensity levels for each consumer COU. EPA incorporated uncertainty and confidence in consumer scenarios into the overall risk estimate confidence scores in Section 4.3.2.4.
SACC	**SACC COMMENTS:** Recommendation: Better organize the discussion on assumptions and uncertainties in Section 4.3 and summarize (tabulate) more of the exposure and hazard uncertainties in this section rather than referring to previous sections. The uncertainty and data limitation sections lack balance, are incomplete, and should be expanded. • More than 2 pages are devoted to exposure and only one paragraph to human health hazard (p. 350). The issues of greatest uncertainties/limitation pertaining to human hazard should be highlighted here, rather than referring the reader to Section 3.2.6. • The summary of uncertainties is too limited (reader is referred to Section 2.3.1.3). One would expect to see a complete summary of uncertainties in this section. A table format would be helpful. • Concerns and issues with congenital heart defects as a non-cancer endpoint are ignored in this section and should be summarized. • Uncertainties in exposure and hazard estimates translate into uncertainties in the risk characterization. A recurrent issue in this	EPA is considering different formats for presenting uncertainty in risk estimates. The SACC proposed varying options without consensus, and EPA will need to determine the most efficient yet informative way to incorporate uncertainties across the different aspects of the risk evaluation. These changes may be incorporated into future risk evaluations.

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	draft risk evaluation is lack of transparency about how the uncertainties and sensitivity analysis get integrated into a balanced evaluation of uncertainty in risk characterization. The Committee believes that an integrated evaluation of uncertainty in the risk characterization would be valuable. This involves risk propagation of uncertainties across the characterization of risk done at least semi-quantitatively (*e.g.,* high, medium, low) with accompanying statements of why each is rated as it is. The summary table should provide annotation and an integrated, semi-quantitative description of uncertainty in the risk characterization. • One Committee member suggested using confidence summary slides similar to Slide #48 in the EPA OPPT technical presentation to SACC; other Committee members indicated that other slides in this presentation (# 13, 24, 27) were useful and should be included in the risk evaluation. • Section 3.1.7 has a more detailed discussion of uncertainties and limitations in environmental hazard identification than that provided in Section 4.3.1. One Committee member suggested either expanding Section 4.3.1 or cross-referencing much of Section 4.3.1 back to Section 3.1.7. • More discussion is needed on the uncertainties in the PBPK model including route-to-route extrapolation (oral to inhalation).	
SACC	**SACC COMMENTS:** Recommendation: Integrate sensitivity analysis findings with the discussion of uncertainties. • Although confidence summaries are presented clearly, it is less clear how assumptions and uncertainties are weighted to arrive at overall confidence summaries. The validity of confidence summaries is difficult to assess without a numerical measure of uncertainty and/or finding from a sensitivity assessment. • The Committee recommends that the draft risk evaluation consider uncertainty and sensitivity analyses concurrently. For instance, a finding with high uncertainty but low sensitivity suggests the lack of	EPA does account for the sensitivity of risk conclusions (*i.e.,* relative to benchmark) to variance across the absolute risk estimates in Section 4.3.2.4. Confidence in risk estimates incorporates the "totality of uncertainties, including confidence levels for each exposure scenario/COU, strength of the human health hazard information, and range of risk estimates provided for the different aspects of the risk evaluation relative to the benchmark."

	confidence in the estimate for a parameter that has little impact on the ultimate risk estimate, whereas a result with medium uncertainty but high sensitivity suggests that the large associated variability for an impactful parameter implies large uncertainty in the final risk. In the latter case, there is greater need to get better information on the parameter to decrease uncertainty in the final risk. This recommendation is valid for the entire risk evaluation, given the degree of uncertainty and data gaps encountered.	
PESS – intrinsic susceptibility (gender/age/genetics/health, etc.)		
SACC	**SACC COMMENTS:** Recommendation: Provide more information for risk assessment of susceptible populations with non-alcoholic fatty liver disease or non-alcoholic steatohepatitis because a large proportion (>30%) of the general population is obese or overweight and have higher levels of fat in their body. Numerous factors including race/ethnicity, life stage, sex differences, lifestyle, nutrition, genetic polymorphisms, and pre-existing health conditions (*i.e.,* obesity, kidney and liver disease) could affect the susceptibility of exposed persons but no substantive discussion is found on susceptible subpopulations in Section 2.3.3. For example, large amounts of fat in the liver may change the toxicokinetics of TCE.	EPA has added non-alcoholic fatty liver disease as a PESS factor in Section 3.2.5.2, and those other factors are also listed as PESS considerations. Section 2.3.3. deals with exposure PESS considerations (*i.e.,* higher exposure) as opposed to biological susceptibility.
SACC	**SACC COMMENTS:** Recommendation: Provide a more detailed risk assessment focused on susceptible subpopulations, particularly pregnant women, their developing fetuses, and people with specific health conditions. Section 3.2.5.2 of the draft risk evaluation provides few details on identified susceptible populations, including pregnant women their developing fetuses, and people with kidney and liver illness. TSCA-relevant potentially exposed sub-populations within workers, ONUs, consumers, product users and bystanders associated with consumer use are also addressed. It is not clear to all Committee members that risks to PESS are adequately covered by the uncertainty factors applied. When are expected PESS responses great enough to require explicit risk	EPA has added a paragraph to Section 4.4.1 acknowledging PESS considerations that could not be directly accounted for in risk estimations and the uncertainty around whether the 99th percentile outputs of the PBPK model sufficiently account for all susceptible subpopulations. EPA has quantified risk estimates for particular PESS groups when possible, including susceptible mothers, those with increased enzymatic activity, and pre-existing infection. Additionally, risk estimates

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	calculations or additional uncertainty factor adjustments? A more accurate estimation of risk to potentially exposed and susceptible sub-populations should be obtained by aggregating exposures with other factors.	were provided for three developmental endpoints in order to account for the PESS group of pregnant mothers and women of childbearing age. Consideration of aggregate exposures are provided in Section 4.4.2. As stated above, EPA acknowledges that the PBPK model cannot account for the entirety of human variability, however the 99th percentile output of the model (based on parameters that can be accounted for) was used for risk estimates to account for the most susceptible proportion of the population. EPA acknowledges that the model does not contain a fetal compartment and the uncertainty this adds in Section 3.2.6.2. While EPA used average adult worker values for exposure estimates, as stated above EPA used toxicity values based on the most toxicokinetically sensitive 1% of the population. Presentation of dermal exposure estimates for women of childbearing age would not have had any effect on risk determination for any occupational Condition of Use, all of which presented Unreasonable Risk (except for Distribution which is covered by regulations for Transportation of hazardous chemicals).
SACC	**SACC COMMENTS:** Recommendations: (1) Provide more details to support the conclusion that the 99th percentile for human equivalent concentration/dose (HEC99/HED99) is sufficient to account for the susceptible populations. (2) Run the PBPK model to understand effects on individuals with abnormal values from pre-existing health conditions such as obesity and hepatitis. Section 4.4.1 includes approximate differences between some groups and what is accounted for in the PBPK model. EPA assumes that by relying on "the 99th percentile output of the PBPK model, [the HEC99/HED99 POD values] are expected to be protective of particularly susceptible subpopulations," but no further discussion is provided. The draft risk evaluation should mention that the PBPK model does not account for pregnancy or lactation. Further, the Fisher PBPK models for fetal component should be included. Although the draft risk evaluation discusses uncertainties with respect to susceptible populations, the Committee was unable to find where the draft risk evaluation quantitatively assesses the impacts of sensitivity to assumption and related uncertainty on risk estimates for susceptible populations.	
56, 108	**PUBLIC COMMENTS:** EPA insufficiently considered the susceptibility of pregnant women and the developing fetus. Under TSCA, EPA has a mandate to protect vulnerable populations. • The prevalence of pregnant women and their fetuses is 4 million per year in the U.S (including 1% with a congenital heart defect). • Dermal risk estimates were presented only for average adult workers, since exposures between this population and women of childbearing age vary by only about 10% (considered by EPA to be	

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	relatively insignificant). EPA must use exposure values applicable to subpopulations with elevated exposure, even if EPA believes that the overall risk conclusion would not be impacted. Ignoring these data fails to identify actual risks to potentially exposed or susceptible populations and makes it more likely that EPA will not identify unreasonable risk where it should or to address that risk in subsequent regulation under TSCA section 6. Ignoring risk deemed "relatively insignificant" also fails to consider the contribution of such risks to overall risks faced by individuals or subpopulations from additional exposures they experience.	
56, 108	**PUBLIC COMMENTS:** EPA did not sufficiently acknowledge that TCE can readily cross the blood-brain barrier. The 2019 ATSDR Toxicological Profile for TCE states: "Trichloroethylene crosses the blood-brain barrier, and the extent of transfer could possibly be greater in young children, although trichloroethylene is expected to readily cross the blood-brain barrier in all age groups." This is essential to emphasize given the evidence for neurotoxicity, including developmental neurotoxicity.	EPA discusses neurological effects of TCE as well as developmental neurotoxicity, both involving central nervous system dysfunction. Therefore, the Risk Evaluation makes it clear that TCE can impact the brain.
56, 73, 108	**PUBLIC COMMENTS:** EPA should acknowledge additional PESS, including individuals with compromised liver or kidney function, cardiac arrhythmias, obesity (based on distribution of TCE to body fat and liver), multiple chronic conditions (*e.g.,* heart, kidney, and liver disease), and co-exposures to other chemicals that interact with TCE metabolism (*e.g.,* chlorinated hydrocarbons, ethanol, phenobarbital).	In Section 3.2.5.2 EPA describes PESS factors that cover all of the considerations included in the comment including variation in cardiac output, socioeconomic status, increased body mass, non-alcoholic fatty liver disease, and diminished health status in general.
56, 108	**PUBLIC COMMENTS:** EPA did not provide, in adequate detail, the extent of genetic variation in key metabolic pathways, which contributes to human susceptibility to TCE toxicity. Further information on and analysis of the potential variability in CYP oxidation across the human population should be provided (including quantitative information when possible).	In Section 3.2.5.2 EPA discusses various genetic susceptibilities including increased CYP2E1 activity and mutations in the VHL tumor suppressor gene. The section also explains that variation in oxidative and conjugative metabolism is accounted for by the use of the 99th percentile PBPK outputs for risk estimation.

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88	**PUBLIC COMMENTS:** EPA must comprehensively assess exposures to TCE and consider its detrimental impacts on fetal development to protect health, including the health of the most vulnerable among us.	EPA agrees with the commenter. These considerations are discussed in Section 3.2.5.2.
104	**PUBLIC COMMENTS:** Tribes must be considered a potentially exposed or susceptible subpopulation under TSCA, because many factors place them at differential risk due to multiple exposure pathways not experienced by the general population, including diet (*e.g.,* increased fish consumption), substandard housing, less stringent worker safety protocols, and water use (drinking, hygiene, ceremonial, artisanal, subsistence, recreational). For the 1,4-dioxane and hexabromocyclododecane (HBCD) risk evaluations, SACC recommended that specific populations (such as tribal populations) be specially considered and that EPA provide quantitative estimates of extra risks for these populations. Special consideration of tribal lifeways and the resulting multiple exposures must be analyzed to determine the risks that Native Americans face.	Populations exposed through pathways excluded from the risk evaluation were not identified as PESS. EPA disagrees with public and scientific advisory committee comments on the draft risk evaluation that suggest tribal communities should be identified as PESS. TSCA provides EPA with the discretion to identify the PESS that are relevant to the chemical-specific risk evaluation [TSCA section 6(b)(4)(A)]. General population exposure pathways were not included in the scope of the risk evaluation evaluated as discussed in Section 1.4.2. Commenters note that the HBCD risk evaluation identified tribal communities as well as subsistence fishermen as PESS; however, HBCD is classified as a persistent bioaccumulative toxic (PBT) compound and expected to bioaccumulate through the food chain. TCE is not a PBT and has low bioaccumulation potential. Therefore, TCE is not a significant concern for communities with elevated fish ingestion and the consumption of fish along with other trophic transfer pathways were not included in the scope of the risk evaluation. EPA recognizes that Native Americans have unique lifeways and has considered established differences in patterns in relevant exposure

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		pathways (*e.g.,* increased fish consumption). However, general population exposure pathways were not included in the scope of the risk evaluation evaluated as discussed in Section 1.4.2 and a review of reasonably available information did not produce data for establishing a differential experience for the evaluated exposure pathways, namely occupational and consumer activities. An additional statement about the uncertainty associated with subpopulations patterns of use has been added to Section 2.3.2.6.2.
105	**PUBLIC COMMENTS:** OEHHA is concerned that the draft risk evaluation ignores developmental toxicity in the concluding risk determination, despite evidence described in other sections of the report. The draft risk evaluation should protect susceptible subpopulations, including the pregnant woman and her fetus, against health effects for which there is substantial evidence.	EPA has the discretion to make unreasonable risk determinations based on other risk benchmarks or factors as appropriate. EPA's unreasonable risk determination (Section 5) considers multiple risk-based factors, including the uncertainties in the analysis (Section 4.3). In considering the uncertainties surrounding these endpoints, the immune endpoints were determined to be the best overall endpoints for risk conclusions and risk determinations. Pregnant women are discussed as a PESS group throughout the PESS sections of the document, and risk estimates are provided for three developmental endpoints.
PESS – exposure to workers		
56, 108	**PUBLIC COMMENTS:** EPA's risk estimation failed to consider workers with compromised health and active workers with elevated respiratory rates. Assuming that all workers are healthy is counter to the TSCA mandate, which directs	In response to SACC and public comments, EPA used the PBPK model to derive HECs/HEDs for occupational exposure for the two key acute and

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	EPA to protect vulnerable populations.	chronic immunotoxicity studies. These model outputs accounted for elevated breathing rate of workers compared to the default at-rest assumptions of the model. The derived occupational HEC/HED values are provided in Section 3.2.5.4.1, and they were used for occupational risk estimates instead of the default PBPK outputs that were used in the draft risk evaluation. EPA acknowledges that individuals with diminished health status are PESS groups in Section 3.2.5.2.
100	**PUBLIC COMMENTS:** Workers exposed to TCE include women of childbearing age. EPA's failure to consider the latest neurodevelopment toxicity data or to use the available data on fetal cardiac malformations leaves those workers and their children exposed to unreasonable risk.	EPA provides risk estimates for both developmental neurotoxicity and congenital heart defects. While these developmental endpoints present more sensitive PODs, (Fredriksson et al., 1993), (Johnson et al., 2003), there is lower confidence in the dose-response results for those studies. To determine whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions based on information and judgement underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in Section 5.2. It is important to note that the benchmarks for cancer and noncancer risk estimates are not bright lines, and EPA has discretion to make unreasonable risk determinations based on other risk benchmarks or factors as appropriate.
PESS – exposure due to proximity (residence near hazardous waste site, manufacturing facility, spill, etc.)		

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SACC	**SACC COMMENTS:** Recommendation: Include discussion of air emissions, contaminated groundwater, and drinking water in human risk characterization discussion. The draft risk evaluation does not consider the implications of some TCE releases that may result in air emissions, contaminated groundwater, and drinking water that could add to the exposure of TSCA-related populations. Some Committee members continue to state that not including estimates of these exposures is unacceptable in the larger framework of risk assessment. The exclusion of these releases implicitly assumes that these potential exposures result in low and acceptable risks or are appropriately managed. In addition, exclusion makes is impossible to assess cumulative and aggregate risk to worker, ONU, and consumer subpopulations exposed simultaneously via multiple pathways.	During Problem Formulation, EPA acknowledged that general population exposures may occur through air, water, soil, and other environmental pathways. However, in the Risk Evaluation EPA did not include pathways under the jurisdiction of other EPA-administered environmental statutes and associated regulatory programs. EPA identified exposure pathways under other environmental statutes administered by EPA, *i.e.,* the Clean Air Act (CAA), the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA), the Resource Conservation and Recovery Act (RCRA), and the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). As explained in more detail in Section 1.4.2 of the Final Risk Evaluation, EPA believes it is both reasonable and prudent to tailor TSCA Risk Evaluations when other EPA offices have expertise and experience to address specific environmental media, rather than attempt to evaluate and regulate potential exposures and risks from those media under TSCA. EPA believes that coordinated action on exposure pathways and risks addressed by other EPA-administered statutes and regulatory programs is consistent with statutory text and legislative history, particularly as they pertain to TSCA's function as a "gap-filling" statute, and also furthers EPA aims to efficiently use Agency resources, avoid
39	**PUBLIC COMMENTS:** Persons at Camp Lejeune in Jacksonville, NC (now an active Superfund site) are exposed to TCE as a drinking water contaminant and subsequently are at risk for cancer and death.	
49, 99	**PUBLIC COMMENTS:** Some subpopulations are exposed to TCE via multiple pathways simultaneously (*i.e.,* TCE in indoor/outdoor air, consumption of contaminated drinking water, reside near TCE-contaminated National Priority List [NPL] sites). Because their exposures levels are higher than for the general population, they face elevated risks of TCE-related health effects (cancer, fetal heart malformations, immunotoxicity). A comprehensive risk evaluation as required by TSCA would identify and quantify these subpopulations, estimate total exposure, and characterize this increased risk. However, the draft risk evaluation fails to provide this analysis and therefore presents an incomplete picture of TCE's risks to the public.	
56, 74, 108	**PUBLIC COMMENTS:** EPA must identify those who face greater exposure due to proximity to	

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	COUs as a "potentially exposed or susceptible subpopulation" who, due to exposure, may be at greater risk of adverse health effects. Only a passing reference to such exposures was made. EPA acknowledged that consumer exposure was underestimated by failing to consider or aggregate background exposures (specifically mentioning populations living near facilities emitting TCE). EPA does not identify these subpopulations and does not analyze the extent by which living in proximity to COUs (*i.e.,* Superfund sites and disposal sites associated with ongoing or prospective manufacturing, processing, distribution, or use) contributes to greater risk. EPA does not provide a justification for excluding such exposures. EPA should analyze the associated risks to these potentially exposed subpopulations and the environmental pathways that lead to their exposure.	duplicating efforts taken pursuant to other Agency programs, and meet the statutory deadline for completing Risk Evaluations. EPA has therefore tailored the scope of the Risk Evaluation for TCE using authorities in TSCA Sections 6(b) and 9(b)(1). Because stationary source releases of TCE to ambient air are covered under the CAA, EPA did not evaluate emission pathways to ambient air from commercial and industrial stationary sources or associated inhalation exposure of the general population. Because the drinking water exposure pathway for TCE is covered in the SDWA regulatory analytical process for public water systems, EPA did not include this pathway in the risk evaluation for TCE under TSCA. In Problem Formulation, EPA also found general population exposures to TCE via underground injection, RCRA Subtitle C hazardous waste landfills, RCRA Subtitle D municipal solid waste (MSW) landfills, and on-site releases to land from industrial non-hazardous waste and construction/demolition waste landfills are under the jurisdiction of and addressed by other EPA-administered statutes and associated regulatory programs. EPA did not include Superfund on-site releases to the environment (which may lead to vapor intrusion), as they are under the jurisdiction of CERCLA. Lastly, EPA did not include emissions to ambient air from municipal and industrial waste incineration and energy recovery units in the risk evaluation, as they are regulated
65, 74	**PUBLIC COMMENTS:** EPA limits its analysis of PESS to those that might face greater susceptibility. Except for workers and consumers, EPA does not consider whether the general population or specific subpopulations face a greater risk due to greater exposure. EPA does not consider people who work or live near manufacturing, processing, use, or disposal sites, or provide any analysis to the extent to which they are at greater risk. This includes people living near active Superfund sites (731 of which are contaminated with TCE).	
93	**PUBLIC COMMENTS:** Residents of Manufacturers Place, as community members who are at greater risk of adverse health effects from exposure to TCE due to their long-term, sustained exposure to the chemical, qualify as a "potentially exposed or susceptible subpopulation" under TSCA. In addition, Manufacturers Place is a former TCE disposal site, making its residents among those EPA identified as a target subpopulation. They also meet the definition of a potentially exposed or susceptible subpopulation based on their greater susceptibility to harm from TCE, because they, like other members of the greater Ironbound community, are historically low-income, people of color that have been disproportionally exposed	

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	to high levels of pollution with the accompanying potential for increased public health impacts, and often facing problems beyond environmental issues (*e.g.,* health risks and housing challenges). • Over 3,300 facilities with environmental permits are located within the two zip codes that cover Ironbound (source: NJDEP's Data Miner website) • There are >200 facilities that store and use hazardous materials on site; over 70 store large enough volumes to require hazardous chemical inventory forms. • EPA's environmental justice mapping and screening database (EJSCREEN) indicates that Ironbound is in the 80th and 90th percentiles for nearly every environmental justice variable. Because of these high levels of exposures to pollutants, Ironbound residents have greater susceptibility to adverse effects from TCE exposure than the general population. Despite this, EPA's draft risk evaluation ignores risks to those in Manufacturers Place and Ironbound from a known harmful use of TCE by entirely excluding analysis of vapor intrusion. This inadequate treatment of susceptible communities is inconsistent with TSCA mandates and must be corrected.	under section 129 of the Clean Air Act. EPA-OPPT acknowledges that it did not consider background exposure from the environment that workers, ONUs, consumers, or bystanders using products containing TCE might be exposed to in addition to exposures from the conditions of use in the scope of the risk evaluation because there is insufficient information reasonably available as to the likelihood of this scenario or the relative distribution of exposures from each pathway. This may result in an underestimation of risk, and EPA acknowledges that risk is likely to be elevated for individuals who experience TCE exposure in multiple contexts. Additional discussion of this issue has been added to Sections 2.3.2.6.1, 2.3.2.2.1, and 4.4.2. TSCA section 6(b)(4)(A) requires EPA to conduct risk evaluations "to determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other nonrisk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator, *under the conditions of use*." (emphasis added) Therefore, TSCA does require that the identified PESS are linked to a COU. Additionally, EPA did not assess exposures to the general population because these exposure pathways and risks are addressed by other EPA-administered statutes.
104	**PUBLIC COMMENTS:** EPA needs to analyze those PESS that face greater exposure due to their proximity to COUs, particularly disposal. In the draft risk evaluation, EPA did not identify these populations and did not provide any analysis of whether those living in proximity to COUs are at a greater risk due to higher exposure. Many tribal communities live near a disposal site or transfer station. The multiple exposure scenarios associated with proximity to unlined disposal site releases to environmental media must be analyzed so that risk determinations can be made for these vulnerable populations. EPA should identify all populations living near disposal and other waste management sites as PESS. Groups living near existing or proposed NPL sites should also be included.	
108	**PUBLIC COMMENTS:** EPA correctly recognized that a potentially exposed or susceptible	

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	subpopulation may include groups of individuals who experience greater exposures due to their proximity to COUs (*e.g.,* near disposal sites). However, EPA ignores the pathways that lead to enhanced exposure (releases to air, water, and land) and provides no explanation for how risk faced by these subpopulations will be evaluated. EPA largely fails to analyze the risks posed to this PESS. EPA should analyze these subpopulations in the final risk evaluation.	
108	**PUBLIC COMMENTS:** EPA should identify people living near COUs, including disposal sites, as PESS, and these subpopulations should be analyzed in the final risk evaluation.	
108	**PUBLIC COMMENTS:** EPA should identify people living in proximity to sources of contamination (*e.g.,* contaminated groundwater) as potentially exposed or susceptible populations, even if these sites are not linked to a specific COU.	
108	**PUBLIC COMMENTS:** EPA cannot exclude legacy uses and associated disposals. EPA has excluded the pathways leading to this exposure from analysis without providing a rationale for how risks will be evaluated for these subpopulations. • EPA should be analyzing communities who work or live near past manufacturing processing, distribution, or use sites, even if those activities have ceased.	The use of TCE in the past are not "legacy" uses. As described in EPA's Risk Evaluation Rule (82 FR 33726 (July 20, 2017)), a legacy use is an ongoing use of a chemical substance in a particular application where the chemical substance is no longer being manufactured, processed, or distributed in commerce for that application. The example provided in the Rule is insulation, which may be present in buildings after a chemical substance component is no longer being made for that use. EPA did not identify any "legacy uses" or "associated disposals" of trichloroethylene, as those terms are described in EPA's Risk Evaluation Rule, 82 FR 33726 (July 20, 2017). Therefore, no such uses or disposals were added to the scope of the

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		risk evaluation for trichloroethylene following the issuance of the opinion in *Safer Chemicals, Healthy Families v. EPA*, 943 F.3d 397 (9th Cir. 2019). In exercising its discretion under TSCA section 6(b)(4)(D) to identify the conditions of use that EPA expects to consider in a risk evaluation, EPA believes it is important for the Agency to have the discretion to make reasonable, technically sound scoping decisions. EPA did not include legacy disposals, (*i.e.,* disposals that have already occurred), because they do not fall under the definition of conditions of use under TSCA section 3(4).
108	**PUBLIC COMMENTS:** Under Executive Order 12898, EPA is required to ensure that environmental justice is appropriately considered, analyzed, and addressed in the draft risk evaluation and has failed to do so. EPA's identification of potentially exposed and susceptible populations is not sufficient to comply with this order. • EPA must consider the disparate impacts of pollution on "minority populations and low-income populations." • Some subpopulations, including low-income, minority, and indigenous communities are disparately exposed to sources of chemical contamination. • EPA's exclusions of exposure pathways linked to disposal sites and legacy use underestimate exposures of environmental justice communities. EPA must consider whether these communities will face an unreasonable risk of injury from TCE.	TSCA § 6(b)(4)(A) requires that EPA conduct a risk evaluation to "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of cost or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator, under the conditions of use." TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." EPA believes that the

		statutory directive to consider potentially exposed or susceptible subpopulations (PESS) and the statutory definition of PESS inherently include environmental justice populations. Thus, EPA's consideration of PESS in this risk evaluation addresses the requirements of the Executive Order. EPA seeks to achieve the fair treatment and meaningful involvement of any group, including minority and/or low-income populations, in the development, implementation, and enforcement of environmental laws, regulations, and policies. To this end, the Agency has already sought input from specific populations and public health experts in implementing TSCA and will continue to do so. EPA will also consider environmental justice populations in accordance with the Executive Order as it develops risk management actions based on final TSCA section 6(b) risk evaluations.
PPE assumptions and effects on risk estimates		
SACC	**SACC COMMENTS:** Recommendation: Identify COUs having very low expectation of appropriate PPE use and incorporate this information in the risk characterization and final risk determination statements. The Committee continues to be concerned over EPA's inclusion of calculations based on the use of PPE in occupational scenarios when EPA has no confidence that PPE is appropriately used by workers in these scenarios. For example, the likelihood of PPE adherence in commercial use OES is so low that EPA should consider not presenting risk estimates with PPE. Alternatively, these risk estimates could be	EPA has outlined its PPE assumptions in Section 5.1 and EPA's assumptions are described in the unreasonable risk determination for each condition of use, in Section 5.2. EPA does not assume that it is a standard industry practice that workers in some small commercial facilities (*e.g.,* those performing spot cleaning, wipe cleaning, shoe polishing, or hoof polishing; commercial printing and copying) have a

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	presented in a separate section or table that describes clearly why EPA is presenting risks with PPE despite EPA's belief that use of exposure controls is unlikely. EPA needs to explain why PPE and "hierarchy of hazard control" are not better considered as mitigation alternatives in response to a determination of "unreasonable risk."	respiratory protection program or regularly employ dermal protection. Therefore, the use of respirators and gloves is unlikely for workers in these facilities. For the purpose of this Risk Evaluation, EPA makes assumptions about potential PPE use based on reasonably available information and expert judgment. EPA considers each condition of use and constructs exposure scenarios with and without engineering controls and /or PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. Again, while EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgment underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. Additionally, in consideration of the uncertainties and variabilities in PPE usage, including the duration of PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties.
SACC	**SACC COMMENTS:**	A hierarchy of controls is a method for

	Although risks are presented with and without PPE, it is inappropriate to consider these as the universe of possibilities in occupational exposure control. Protective equipment is described and quantified with simple (but usually not supportable) assumptions; however, the hierarchy of controls stipulates that PPE should only be invoked after engineering and administrative controls.	eliminating workplace hazards. While EPA has assessed the extent to which certain exposure reduction tools that it assumes to be in place may be reducing risks to workers, application of the methodology of the hierarchy of controls is not relevant to risk evaluations. EPA will manage unreasonable risks presented by chemical substances when the Agency undertakes regulatory action for COUs determined to have unreasonable risk. Utilization of the hierarchy of controls to recommend or require risk management actions in the risk evaluation would be premature and inappropriate.
SACC	**SACC COMMENTS:** The adequate use of PPE cannot be assumed. Many on the Committee support removing the use of PPE in the risk characterization section. If this is not possible, expectations or evidence of PPE under all COUs, and PPE use impacts on risk characterization should be a separate discussion and tied to tables separate from non-PPE values.	EPA's approach for developing exposure assessments for workers is to use the reasonably available information and expert judgement. When appropriate, in the risk evaluation, EPA will use exposure scenarios both with and without engineering controls and/or PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. Again, while EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgement underlying the exposure scenarios. These

		assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. Additionally, in consideration of the uncertainties and variabilities in PPE usage (*e.g.,* dry cleaners), EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties. EPA has also outlined its PPE assumptions in section 5.1. Further, in the final risk evaluation for TCE, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE. EPA will review how the risk values are presented (PPE vs non-PPE), and determine whether an alternative presentation approach should be taken in future risk evaluations.
SACC	**SACC COMMENTS:** The primary assumption that exposure control recommendations are followed considering evidence to the contrary should be addressed directly. EPA should make a decision as to whether the lack of specific data on PPE use and having no confidence that it is used as recommended results in a decision to not characterize risks with PPE. Alternatively, EPA should transparently and clearly explain why exposure and risk estimates with PPE are provided in all cases despite evidence of poor adherence to such use and EPA's recognition of uncertainty about the proper use of PPE in many scenarios. Is PPE use being considered a COU, or as many of the Committee consider it, a risk modifier?	EPA's approach for developing exposure assessments for workers is to use the reasonably available information and expert judgement. When appropriate, in the risk evaluation, EPA will use exposure scenarios both with and without engineering controls and/or PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. Again, while EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether or not a

		condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgement underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. Additionally, in consideration of the uncertainties and variabilities in PPE usage (*e.g.,* dry cleaners), EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties. EPA has also outlined its PPE assumptions in section 5.1. Further, in the final risk evaluation for TCE, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE.
SACC	**SACC COMMENTS:** • Although PPE and Protection Factors (PFs) have been discussed at length in previous draft risk evaluations reviewed by the SACC, one Committee member raised a new concern that the factor that had the greatest impact on the final risk determination is PPE PFs as categorical constants in risk determination calculations. This reviewer cited the comments by the Environmental Defense Fund (EDF) and their analysis, which indicates that the factor that had the greatest impact on the risk determination was the application of PPE PFs for respirators and gloves. This reviewer noted that the factor that impacts the risk determination the most has only one page of text dedicated to discussion. • EPA must provide an expanded justification for applying various PFs to reduce the risk determination as constants applied to whole populations in the equations. It was hard to discern on p. 120 of the draft risk evaluation that OSHA only requires respiratory PPE be used when the PEL continues to be exceeded after implementing the	EPA appropriately applied the glove PFs within the framework used in the TCE risk evaluation. EPA will consider further refinements to the dermal approaches in future risk evaluations. The hierarchy of controls discussed is a method for eliminating workplace hazards. While EPA has assessed the extent to which certain exposure reduction tools that it assumes to be in place may be reducing risks to workers, application of the methodology of the hierarchy of controls is not relevant to risk evaluations. EPA will manage unreasonable risks presented by chemical substances when the Agency undertakes regulatory action for COUs determined to have unreasonable risk. Utilization of the hierarchy of

	higher priority controls in the exposure control strategy. Assuming that PPE is required for all workers and used continuously is, therefore, not likely to be correct. This leads to the conclusion that application of PFs in risk determination for TCE is inappropriate unless the entire worker group is exposed at levels above the PEL. • EPA's use of these various PFs thus serve to inappropriately and systematically reduce the calculated risk. There is a lack of substantial discussion about exposure controls and use of PPE in actual practice. EPA references some of the NIOSH HHEs and should review those to see what was being done in the businesses inspected by NIOSH and the corresponding exposure levels. Nearly all were below the PEL. Modification of risk estimates by applying PFs for PPE seemed to many on the Committee as inappropriate when there is no regulatory reason to compel the use of such PPE.	controls to recommend or require risk management actions in the risk evaluation would be premature and inappropriate. EPA's approach for developing exposure assessments for workers is to use the reasonably available information and expert judgement. When appropriate, in the risk evaluation, EPA will use exposure scenarios both with and without engineering controls and/or PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. Again, while EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgement underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. Additionally, in consideration of the uncertainties and variabilities in PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties. EPA has also outlined its PPE assumptions in section 5.1. Further, in the final risk evaluation for TCE, EPA has determined that most conditions of use

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		pose an unreasonable risk to workers even with the assumed PPE.
56, 74, 108	**PUBLIC COMMENTS:** EPA assumed universal use and effectiveness of PPE for most COUs throughout the value chain and lifecycle. Workers at any facility where effective use of PPE cannot be documented should be considered vulnerable subpopulations as per TSCA requirements.	For the purpose of this Risk Evaluation, EPA makes assumptions about potential PPE use based on reasonably available information and expert judgment. EPA considers each condition of use and constructs exposure scenarios with and without engineering controls and /or PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. Again, while EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgment underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. Additionally, in consideration of the uncertainties and variabilities in PPE usage, including the duration of PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties. EPA has also outlined its PPE assumptions in Section 5.1 and EPA's assumptions are described in the unreasonable risk determination for each condition of use, in
49, 99	**PUBLIC COMMENTS:** EPA's risk determinations for workers calculate MOEs assuming the use of gloves and respirators and the absence of protective equipment. MOEs for scenarios where workers reliably use PPE are below benchmarks for all COUs; however, EPA's MOEs are significantly lower for no PPE scenarios. As SACC has repeatedly underscored and EPA has recognized, the expectation of universal PPE is contrary to the realities of workplace. As EPA is required to consider 'reasonably foreseen' COUs, and universal PPE use is not reasonably foreseeable, the no PPE scenario is the only defensible baseline for determining risk levels and defining additional worker protections necessary to eliminate risk.	
49, 99	**PUBLIC COMMENTS:** EPA's unreasonable risk determinations for workers should not assume protection via PPE. In each of its reviews of draft risk evaluations, SACC has raised concerns about EPA's reliance on PPE for determinations of unreasonable risk. SACC concluded that assumptions about PPE use are likely unrealistic for many of the scenarios so that risk determinations should be based on no PPE use.	

		Section 5.2. EPA is required to conduct risk evaluations to determine whether chemical substances present unreasonable risk "under the conditions of use," TSCA section 6(b)(4)(A). "Conditions of use" include intended, known, or reasonably foreseen activities associated with a chemical substance, TSCA section 3(4). Occupational exposure scenarios and assumptions are not the same as COUs.
49, 99	**PUBLIC COMMENTS:** EPA's unreasonable risk determinations for workers should not assume that they will be protected by PPE. There is evidence that workers are not meaningfully protected by PPE. • Most worker exposure to TCE is in small, poorly controlled operations. EPA found in its 2017 proposal to ban vapor degreasing that nearly all vapor degreasing "open-top" degreasers [resulted in risk]. • The OSHA PEL is 100 ppm, three orders of magnitude higher than the level that current TCE health effects data warrant. Without a health-protective OSHA limit, it is inconceivable that OSHA is enforcing, or employers are implementing, stringent PPE requirements. In the proposal to ban vapor degreasing, EPA noted that worker comprehension of warnings and labels was poor. Many operations lack effective training and hazard communication programs. Occupational bystanders mat not even encounter warnings and labels.	EPA agrees that there are challenges associated with use of PPE; they are described in section 5.1.1.3. By providing risk estimates assuming use of PPE, EPA is not recommending or requiring use of PPE. EPA's approach for evaluating risk to workers and ONUs is to use the reasonably available information and professional judgment to construct exposure scenarios that reflect the workplace practices involved in the conditions of use of the chemicals and address uncertainties regarding availability and use of PPE. EPA uses exposure scenarios both with and without engineering controls and/or PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. Again, while EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that

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		workers are unprotected. EPA acknowledges that there is a PEL but did not use it as a benchmark for either risk assessment or unreasonable risk determination. EPA provided the PEL as a point of comparison only to help readers understand EPA's workplace exposure and risk estimates compared to a familiar exposure concentration, as expressed in the PEL. EPA did not use the PEL in the development of the risk estimates or as part of making an unreasonable risk determination. TCE is the subject of an OSHA standard. OSHA has established a permissible exposure limit (PEL) of 100 ppm for TCE. However, as noted on OSHA's website, "OSHA recognizes that many of its permissible exposure limits (PELs) are outdated and inadequate for ensuring protection of worker health. Most of OSHA's PELs were issued shortly after adoption of the Occupational Safety and Health (OSH) Act in 1970, and have not been updated since that time." OSHA provides an annotated list of PELs on its website, including alternate exposure levels. For TCE, the alternates provided are the California OSHA PEL of 25 ppm and the ACGIH TLV of 25 ppm. (https://www.osha.gov/dsg/annotated-pels/tablez-2.html). For the purposes of determining whether or not a condition of use presents unreasonable risks,

		EPA incorporates assumptions regarding PPE use based on information and judgment underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2 and in the risk characterization section in Table 4-9. Additionally, in consideration of the uncertainties and variabilities in PPE usage, including the duration of PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties.
56, 69, 74, 108	**PUBLIC COMMENTS:** EPA's risk determination relied on unsupported assumptions that workers will use PPE and that it will be universally effective. EPA states that risk determinations "incorporate consideration of expected PPE" (frequently a respirator of an assigned protection factor [APF] 25 or 50 and gloves with PF 5-20.) Statements that there are little to no actual data on PPE use are provided only in the Supplemental File: Environmental Releases and Occupational Exposure. While EPA still finds unreasonable risk for most COUs, PPE assumptions dramatically underestimate the extent and magnitude of risks (both in cases where EPA did find a COU presented an unreasonable risk and in cases where it did not). Worker exposure to TCE in the absence of PPE must be considered reasonably foreseen.	EPA's approach for developing exposure assessments for workers is to use the reasonably available information and expert judgement. When appropriate, in the risk evaluation, EPA will use exposure scenarios both with and without engineering controls and/or PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. Again, while EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgement underlying the exposure scenarios. These

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		assumptions are described in the unreasonable risk determination for each condition of use, in section 5.3.
56, 69, 74, 108	**PUBLIC COMMENTS:** EPA assumed without evidence that respirators or glove use would result in levels of protection based on hypothetical PPE scenarios. The reliance on PPE does not reflect the best available science and policy. • EPA only identified unreasonable risk when the most stringent PPE use (to protect against inhalation and dermal exposures) was insufficient to mitigate risk or when EPA could not justify any assumption that PPE would be used. • EPA relies on PPE despite evidence of its limitations. For example, OSHA notes limitations associated with respirator use (*e.g.,* fit, physiological burden). • EPA's reliance on PPE is counter to OSHA's Hierarchy of Controls (HOC), which prioritizes measures to reduce or eliminate the presence of a hazard over measures that place the burden on the worker (warning labels and reliance on PPE). During the TCE SACC meeting, a peer reviewer noted that measures higher up in the HOC, including whether a chemical is needed at all as well as protection afforded by engineering controls, should be considered first. The HOC puts PPE as the last resort.	The hierarchy of controls is a method for eliminating workplace hazards. While EPA has assessed the extent to which certain exposure reduction tools that it assumes to be in place may be reducing risks to workers, application of the methodology of the hierarchy of controls is not relevant to risk evaluations. EPA will manage unreasonable risks presented by chemical substances when the Agency undertakes regulatory action for COUs determined to have unreasonable risk. Utilization of the hierarchy of controls to recommend or require risk management actions in the risk evaluation would be premature and inappropriate. EPA's approach for developing exposure assessments for workers is to use the reasonably available information and expert judgement. When appropriate, in the risk evaluation, EPA will use exposure scenarios both with and without engineering controls and/or PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. Again, while EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For

		the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgement underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. Additionally, in consideration of the uncertainties and variabilities in PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties. EPA has also outlined its PPE assumptions in section 5.1. Further, in the final risk evaluation for TCE, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE.
56, 108	**PUBLIC COMMENTS:** EPA frequently assumes that PPE is also used and effective in order to find no unreasonable risk to workers even though EPA also states that it does not have data on use/effectiveness of gloves or the existence of comprehensive respiratory protection programs.	EPA's approach for developing exposure assessments for workers is to use the reasonably available information and expert judgement. When appropriate, in the risk evaluation, EPA will use exposure scenarios both with and without engineering controls and/or PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. Again, while EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether or not a

		condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgement underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. Additionally, in consideration of the uncertainties and variabilities in PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties. EPA has also outlined its PPE assumptions in section 5.1. Further, in the final risk evaluation for TCE, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE.
56, 108	**PUBLIC COMMENTS:** Analysis of the risk estimates summarized in EPA's Table 4-54, performed to characterize the impact of EPA's PPE assumptions, found that: • EPA identified a risk estimate for a COU represented an unreasonable occupational risk only when the risk estimate was so high that it could not go away even after assuming workers would use the most protective PPE that EPA considered or where EPA could not assume any use of respirators. • For nearly all COUs where EPA found that its risk estimates for acute, chronic, or cancer risks to workers did not represent an unreasonable risk, in order to reach that finding, EPA had to assume that all of the workers were using PPE. • Even where EPA did find unreasonable risk to workers, EPA has grossly understated both the extent and magnitude of those risks by assuming use of PPE.	EPA's approach for developing exposure assessments for workers is to use the reasonably available information and expert judgement. When appropriate, in the risk evaluation, EPA will use exposure scenarios both with and without engineering controls and/or PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. Again, while EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether or not a condition of use presents unreasonable risks,
56, 69,	**PUBLIC COMMENTS:**	

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74, 108	EPA's assumption that PPE use is universally used and effective results in risk estimates not being carried into final risk determinations and subsequently regulated, forgoing EPA's only opportunity to ensure PPE is used and workers are protected. Although EPA finds all occupational COUs present unreasonable risk, risk estimates that are understated because of PPE assumptions means that subsequent regulation EPA promulgates under TSCA will be under-protective. The magnitude of underestimation is large even using EPA's 500-fold more lenient immunosuppression endpoint (16-, 34-, and 23-fold for acute, chronic, and cancer risks, respectively) based on detailed analyses of COUs, exposure routes (inhalation and dermal), and exposure levels (high-end or central tendency) for acute, chronic, and cancer risks.	EPA incorporates assumptions regarding PPE use based on information and judgement underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. Additionally, in consideration of the uncertainties and variabilities in PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties. EPA has also outlined its PPE assumptions in section 5.1. Further, in the final risk evaluation for TCE, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE.
80	**PUBLIC COMMENTS:** By assuming 100% compliance with and effectiveness of PPE, EPA miscalculates risks to workers (a conclusion supported by SACC). OSHA inspection results indicate that this level of PPE adherence is not achieved in workplaces that use TCE, as evidenced by citations to the Automotive Body, Paint, and Interior Repair and Maintenance citations (in 2018 and 2019), an industry classification that overlaps with TCE with respect to occupational exposure scenarios. In addition, a recent study of workplace safety practices in the auto collision industry found declines in respiratory protection and right-to-know training.	
100	**PUBLIC COMMENTS:** For all but 5 of 29 occupational COUs, EPA assumes that all directly exposed workers are provided appropriate PPE along with the fit testing, medical examinations, and training required to properly use such equipment. EPA assumes that workers will universally wear respirators with an average PF of up to 50 and chemical-resistant gloves with a protectiveness factor of up to 20. Even where EPA finds unreasonable risk, it calculates the workers' MOEs and cancer risks based on its assumption of PPE use, such that any subsequent regulations of TCE under TSCA will not be sufficient to protect those workers who are not provided with or cannot consistently use PPE.	

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100	**PUBLIC COMMENTS:** EPA's assumption of PPE use violates TSCA's requirement to use the best available science, since the best available science for occupational risk assessment requires measurements of worker exposures and risks without PPE. These non-PPE measurements permit OSHA and other agencies to determine whether risks can be mitigated via engineering controls and hazard elimination before the consideration of PPE, consistent with the occupational hierarchy of controls.	
100	**PUBLIC COMMENTS:** EPA's PPE assumptions conflate risk evaluation and management. TSCA requires EPA to complete a risk evaluation and to make determinations of unreasonable risk before it considers how those risks be managed. PPE may be considered, if at all, only during the risk management stage. By assuming PPE use at the risk evaluation stage, EPA ignores the significant limitations on widespread PPE use. Because EPA need only regulate TCE to eliminate unreasonable risks, the inclusion of PPE in risk evaluations means that subsequent TSCA regulations will not protect workers who do not use PPE. EPA's assumption of PPE preempts the required consideration of alternate regulatory tools during the risk management stage.	
102	**PUBLIC COMMENTS:** EPA makes several assumptions regarding the need for, and the use of, PPE. Those assumptions often do not include the use of all PPE as required by NIOSH and/or EPA. The automotive industry maintains procedures and worker requirements that meet or exceed the recommended safety protections and PPE. It is therefore important that EPA base its risk evaluations on manufacturing scenarios where the automotive sector is fully utilizing all required PPE.	
104	**PUBLIC COMMENTS:** EPA has significantly underestimated occupational exposures by assuming proper use of effective PPE without evidence. OSHA has informed EPA that respirators are the least satisfactory approach to exposure control, and the SACC report on 1,4-dioxane expressed	

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	concern that smaller facilities are less likely to require routine PPE use or to employ engineering controls. Tribal communities, in particular, often have smaller facilities and are subject to OSHA exemptions and OSHA reporting and inspection requirements. In the case of TCE, EPA found unreasonable risk to workers for all COUs considered. However, EPA's risk determination is based on assumptions that workers will use PPE (both gloves and respirators) at most times when working with TCE, which means that actual risks to workers are substantially underestimated. A risk analysis for workers without PPE also must be included. For accurate risk characterization of tribal members, NTTC would like to see a risk determination for workers and ONUs, both self-employed and in small businesses, that incorporates OSHA's exemptions and practical exceptions. In these communities, take-home exposures are also likely.	
PPE – respirator/APF assumptions are not valid		
49, 99	**PUBLIC COMMENTS:** EPA's proposal to ban vapor degreasing conceded that respirators could not be relied on to protect TCE-exposed workers owing to documented limitations to successful implementation (including individuals with impaired lung function, problems associated with adequate fit, and issues with respect to communication, vision, fatigue, and decreased efficiency). In addition, there are difficulties with implementing an effective respirator program (which requires training, respirator selections, medical evaluations, etc.) in small establishments.	The purpose of risk evaluation under TSCA is "to determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other nonrisk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator, under the conditions of use." TSCA section 6(b)(4)(A). Implementation of respiratory protection programs at facilities is not a component of a risk evaluation under TSCA.
56, 108	**PUBLIC COMMENTS:** Assumptions that respirators are effective are unsupported. Exposure to TCE may occur even when respirators are used, and this may occur without providing any indication to the user that it is no longer functioning.	EPA assumes for some conditions of use, the use of appropriate respirators is not a standard practice, based on best professional judgment given the burden associated with the use of

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		supplied-air respirators, including the expense of the equipment, and the necessity of fit-testing and training for proper use. The risk evaluation also presents estimated risk in the absence of PPE and does not assume that occupational non-users use PPE.
100	**PUBLIC COMMENTS:** EPA improperly assumes the use of respirators by workers exposed to TCE. EPA identifies no data concerning the respirator use, but rather relies on a 2003 NIOSH survey of respirator use across private sector employers. This survey directly undermines EPA's PPE assumptions. With respect to the TCE draft risk evaluation, an EPA risk assessor indicated that the NIOSH study highlights the potential uncertainty associated with widespread use of respiratory protective equipment. In addition, respirators cannot be assumed to be protective even when they are used (as this is dependent on fit, training, and other factors). Therefore, EPA cannot assume that workers provided respirators will be adequately protected. EPA has previously acknowledged limitations on respirator use in its December 2016 proposal to ban aerosol degreasing uses of TCE. However, EPA now assumes that all workers exposed to TCE from aerosol degreasing will be provided with and protected by APF 50 respirators. OSHA and NIOSH have likewise indicated that there is only a "nominal possibility" that respirators will be worn properly owing to the limitations of their use (heat stress, discomfort, and other hazards). Because EPA is required to evaluate chemicals as it is "reasonably seen" to be manufactured, processed, distributed, used, or disposed, EPA must make risk determinations about TCE use under the foreseen and known circumstances where respirators are not worn.	EPA has outlined its PPE assumptions in section 5.1 and has supplemented some sources and information on respirator use in Section 2.4.1.1. of the Risk Evaluation and Section 1.4.6 of the Supplemental Information on Releases and Occupational Exposure Assessment. EPA has also added a table in Section 4.2.2.1 to make the PPE assumptions made for each COU clearer. For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgment underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. Additionally, in consideration of the uncertainties and variabilities in PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties.
108	**PUBLIC COMMENTS:** EPA completely failed to acknowledge data on respirator use into the draft risk evaluation. The SACC Peer Review Report on Methylene Chloride recommended that EPA incorporate data from the NIOSH and Bureau of Labor Statistics joint survey on "Respirator Usage in Private	The risk evaluation does acknowledge the work completed by NIOSH and the BLS on respirator use in Section 2.3.1.2.6.

	Sector Firms," which provides industry estimates of respirator program effectiveness and additional data from other published sources. Based on these data, it was concluded in the draft carbon tetrachloride risk evaluation that "the likelihood of respirator use may not be widespread."	
PPE – glove assumptions are not valid		
56, 108	**PUBLIC COMMENTS:** Assumptions that gloves are effective are unsupported. Gloves may provide limited protection from TCE exposure, and protection varies based on glove materials. EPA does not provide data on the effectiveness of gloves, assumes default glove PFs, and disregards the potential for occlusion to increase exposure.	EPA's approach for developing exposure assessments for workers is to use the reasonably available information and expert judgement. EPA considers each condition of use and uses exposure scenarios with and without PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on this information and judgment underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.3. While EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. In consideration of these uncertainties and variabilities in PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties. Assumptions for glove PFs are based on (Marquart et al., 2017).

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56, 108	**PUBLIC COMMENTS:** EPA used default glove PFs (5x, 10x, and 20x), ignoring the elevated dermal exposures of workers in occluded scenarios. EPA does this without empirical data to account for the complexities of glove use (*e.g.,* contamination or increased absorption due to increased skin temperature). EPA fails to acknowledge the uncertainties and deficiencies in its glove use assumptions in the Risk Determination section of this draft risk evaluation. • For consumers, EPA fails to consider improper glove use and its potential to lead to occlusion and potentially higher exposure than the no gloves/soaked rag assumption on which EPA relies. • For workers, glove limitations are acknowledged but 5x, 10x, or 20x PFs are still assumed despite the potential for occlusion and in the absence of evidence. In cases where EPA did not identify unreasonable risks based on the assumption of glove use, risks to workers will occur whenever a worker uses anything less than the assumed gloves or when there is occlusion.	See further discussion on occlusion in Section 2.3.1.1 of the Risk Evaluation and Appendix H of the Supplemental Information on Releases and Occupational Exposure Assessment document. The occluded scenarios were presented as a what-if scenario. EPA does not know the likelihood or frequency of these scenarios in the workplace; therefore, EPA did not present risk estimates associated with occluded exposure in the Risk Evaluation however a breakdown of the exposure scenarios for which this was considered can be found int the [*Risk Calculator for Occupational Exposures. Docket: EPA-HQ-OPPT-2019-0500]*. EPA has acknowledged in Section 4.3.2.1 that risks under occluded exposure conditions may be higher than estimated under no-glove conditions.
94	**PUBLIC COMMENTS:** EPA's approach of applying a glove PF is appropriate for accounting for contact with a gloved hand. However, the PFs should be applied to the non-occluded ungloved estimates following a revised analysis, not the original estimates presented in the risk assessment (which were likely 6- to 17-fold too large).	EPA appropriately applied the glove PFs within the framework used in the TCE risk evaluation. EPA will consider further refinements to the dermal approaches in future risk evaluations. EPA used the best available science and reasonably available data to assess exposures for each COU. EPA appreciates any additional data from commenters that would improve its estimates of occupational exposures.
99	**PUBLIC COMMENTS:** EPA's assumption that gloves will provide any level of protection is speculative. EPA acknowledges that there are limited data on glove use and admitted in other evaluations that glove PFs are highly uncertain. Even when used, gloves may not be effective (some types lack	EPA considers each condition of use and uses exposure scenarios with and without PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. For the

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	impermeability for certain chemicals or fail to fully prevent exposure). There are scenarios in which glove use may increase skin absorption. The draft risk evaluation states that "dermal exposure may be significant in cases of occluded exposure." Risk determinations for PPE scenarios are based on default glove PFs and do not reflect the increase from glove occlusion scenarios. This is a serious omission. If EPA assumes glove use in the final risk evaluation (and it should not), EPA must also base in its risk determinations on the foreseeable occlusion scenarios that glove use would create.	purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on this information and judgment underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.3. While EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. In consideration of these uncertainties and variabilities in PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties. As stated in a previous response, EPA does not know the likelihood or frequency of these scenarios in the workplace; therefore, EPA did not present risk estimates associated with occluded exposure in the Risk Evaluation. EPA has acknowledged in Section 4.3.2.1 that risks under occluded exposure conditions may be higher than estimated under no-glove conditions.
100	**PUBLIC COMMENTS:** EPA improperly assumes that all workers will use protective gloves, even though they acknowledge that data to support this assertion are limited. • Absent a recognized dermal hazard, OSHA does not mandate glove use. • EPA has no information on how many workers who are exposed	EPA's approach for developing exposure assessments for workers is to use the reasonably available information and expert judgement. When appropriate, in the risk evaluation, EPA will use exposure scenarios both with and without engineering controls and/or PPE that

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	wear gloves, or how protective such gloves would be if worn. • If gloves are provided, EPA has little to no information about the types of gloves worn, a critical omission given that not all gloves are protective against TCE. • SDS recommendations are not binding. EPA has no basis for assuming specific glove PFs. The TSCA SACC notes that improper glove use can also lead to increased worker exposures due to contamination on the inside surface (if workers are not properly trained) or by "acting as a reservoir" for contaminants (if the gloves are not impermeable). EPA notes that the effectiveness of gloves is dependent upon training but provides no data about training programs. In the draft risk evaluation, EPA conducts a separate glove "occlusion" analysis, which found dermal exposures up to several fold higher than under no-glove scenarios. In its final risk calculations, however, EPA ignores the foreseeable exposure scenarios in which employees are not provided protective gloves, or are provided inadequate gloves or are not adequately trained and thus face even greater dermal exposures due to glove contamination and the occlusion of TCE close to the skin. EPA's assumption that all workers will be properly wear chemical-resistant gloves is unfounded and contrary to TSCA.	may be applicable to particular worker tasks on a case-specific basis for a given chemical. Again, while EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgment underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. Additionally, in consideration of the uncertainties and variabilities in PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties. EPA has also outlined its PPE assumptions in section 5.1. Further, in the final risk evaluation for TCE, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE.
Interpretation of OSHA requirements for PPE		
49, 99	**PUBLIC COMMENTS:** EPA repeatedly suggested that OSHA regulations obligate employers to implement PPE where necessary to provide protection against chemical risks. OSHA regulations do not require employers to follow the recommendations in an SDS, and the preamble to OSHA's hazard communication rule expressly states that "there is no requirement for employers to implement the recommended controls." Moreover, OSHA	For the purpose of this Risk Evaluation, EPA makes assumptions about potential PPE use based on reasonably available information and expert judgment. EPA considers each condition of use and constructs exposure scenarios with and without engineering controls and /or PPE

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	regulations give employers latitude to interpret evidence of workplace risks and to select worker protection measures they deem appropriate. There is no evidence that employers uniformly implement PPE or workplace controls sufficient to eliminate these risks in the absence of any legal obligation to do so. In addition, the draft risk evaluation explains OSHA's HOC for protecting workers. Consistent with the HOC and the SACC's consistent recommendations, EPA's risk determinations should assume no PPE use. How to eliminate TCE's unreasonable risks to workers should be decided in the TSCA risk management phase and PPE should be considered as a last resort, only after other means of control such as chemical substitution and engineering controls have been shown to be inadequate.	that may be applicable to particular worker tasks on a case-specific basis for a given chemical. Again, while EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgment underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. Additionally, in consideration of the uncertainties and variabilities in PPE usage, including the duration of PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties.
56, 80, 108	**PUBLIC COMMENTS:** EPA mischaracterizes OSHA regulations (29 CFR § 1910.134) throughout the draft risk evaluation. • The OSHA PPE standard is rendered unprotective by the outdated TCE PEL; OSHA cannot require respirators at TCE levels below the 100 ppm PEL. The OSHA respiratory protection standard requires an entire program (*i.e.,* fit testing and medical exams) if respirators are provided; therefore, there is a disincentive. • OSHA regulations do not require compliance with SDSs (which are non-binding). Not only do OSHA regulations not require compliance (but rather leaves this decision to the employer), but even if mandatory, reliance on them would be insufficient to ensure protection because SDSs are often inaccurate, incomplete, and too technical for many workers to understand. OSHA's database of inspections demonstrates significant non-compliance with respiratory protection requirements such as those that apply to TCE. Cal/OSHA submitted comments to the TCE docket indicating that an industry classification with many of the same occupational exposure scenarios covered by the TCE draft risk evaluation (Automotive Body, Paint, and Interior repair and Maintenance; North American Industry Classification System [NAICS]	

	Code 81121) was the second most cited for respiratory protection in 2018.	
61	**PUBLIC COMMENTS:** OSHA's hierarchy of controls is clear that it is unacceptable to use PPE as the primary means to protect workers; rather, the most effective way to control hazards is through engineering controls. EPA's draft risk evaluation bases hazard estimates on the assertion that workers will be protected from exposure via PPE use. The underlying assumptions (which are likely not true) are that workers will be provided PPE, that workers will be able to properly use PPE (having no medical conditions that preclude use), and that PPE will be effective. Recommendations in SDSs are not required to be followed by employers under OSHA, and many employers do not follow recommendations and/or OSHA legal requirements. Existing OSHA regulations will not result in appropriate PPE use. EPA continues to produce risk evaluations that ignore long-standing worker protection policies. EPA's risk draft evaluation assumes that employers will offer PPE when there are incentives not to (*e.g.,* expense of medical monitoring, fit testing requirements). Despite this, EPA assumed PPE use, leading to incorrect estimates of exposure, and drastically underestimating risks by order of magnitude. EPA must go back and make determinations of unreasonable risk assuming that many workers will not be using appropriate PPE.	Section 2.3.1.2.6 of the Risk Evaluation discusses the hierarchy of controls and that PPE is the last stage of protection. EPA considers each condition of use and uses exposure scenarios with and without PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on this information and judgment underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.3. While EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. In consideration of these uncertainties and variabilities in PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties.
100	**PUBLIC COMMENTS:** EPA improperly assumes the use of respirators at levels far below the TCE permissible exposure limit. EPA is simply wrong to assume that employers have a duty under OSHA to provide PPE to workers at	EPA agrees that there are challenges associated with use of PPE; they are described in section 5.1.1.3. By providing risk estimates assuming use

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	exposure levels below 100 ppm and EPA has no evidence to suggest that employers voluntarily do so. OSHA does not require workers to be provided with or to use PPE when exposures fall below the PEL, and EPA cites no evidence that workers have or will voluntarily provide expensive and burdensome PPE in circumstances where OSHA does not require it. Respirators with an APF of 50 are often bulky, inhibit a worker's ability to safely do their job, and require extensive fit testing, medical examinations, filter change schedules, cleaning, and maintenance. EPA nowhere accounts for these serious limitations in the practical use of, or employer willingness to supply this type of PPE.	of PPE, EPA is not recommending or requiring use of PPE. EPA's approach for evaluating risk to workers and ONUs is to use the reasonably available information and professional judgment to construct exposure scenarios that reflect the workplace practices involved in the conditions of use of the chemicals and address uncertainties regarding availability and use of PPE. EPA uses exposure scenarios both with and without engineering controls and/or PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. Again, while EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. EPA acknowledges that there is a PEL but did not use it as a benchmark for either risk assessment or unreasonable risk determination. EPA provided the PEL as a point of comparison only to help readers understand EPA's workplace exposure and risk estimates compared to a familiar exposure concentration, as expressed in the PEL. EPA did not use the PEL in the development of the risk estimates or as part of making an unreasonable risk determination. Information reasonably available to EPA, including data submitted by chemical manufacturers and processors, indicates that PPE
100	**PUBLIC COMMENTS:** EPA relies on OSHA's Hazard Communication Standard to support its expectation that workers will be provided appropriate PPE consistent with applicable SDSs; however, employers are not obligated under OSHA to follow SDS recommendations. In addition, information in SDSs is often vague and inconsistent so that they are not effective hazard communication tools. In the absence of a requirement for employers to implement the recommended controls, there is no basis in EPA's assumption that the Hazard Communication Standard will result in uniform use of appropriate PPE.	

		is generally used. EPA does not assume that the inclusion of PPE on SDSs is sufficient to ensure PPE use. While EPA considers the information on SDSs, EPA does not make PPE use assumptions based solely on SDSs. TCE is the subject of an OSHA standard. OSHA has established a permissible exposure limit (PEL) of 100 ppm for TCE . However, as noted on OSHA's website, "OSHA recognizes that many of its permissible exposure limits (PELs) are outdated and inadequate for ensuring protection of worker health. Most of OSHA's PELs were issued shortly after adoption of the Occupational Safety and Health (OSH) Act in 1970, and have not been updated since that time." OSHA provides an annotated list of PELs on its website, including alternate exposure levels. For TCE, the alternates provided are the California OSHA PEL of 25 ppm and the ACGIH TLV of 25 ppm. (https://www.osha.gov/dsg/annotated-pels/tablez-2.html). For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgment underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2 and in the risk characterization section in Table 4-9. Additionally, in

		consideration of the uncertainties and variabilities in PPE usage, including the duration of PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties.
Human health risk characterization		
SACC	**SACC COMMENTS:** The Committee recommends that the evaluation base the risk characterization on aggregation of inhalation and dermal risks.	EPA has added to the discussion of aggregate and sentinel exposures in Section 4.4.2. In short, without a PBPK model containing a dermal compartment to account for toxicokinetic processes the true internal dose for any given exposure cannot be determined. Aggregating exposures could inappropriately overestimate total exposure, as simply adding exposures from different routes without an available PBPK model for those routes would compound uncertainties.
SACC	**SACC COMMENTS:** Recommendation: Risks from oral exposures should be discussed and its exclusion justified in the draft risk evaluation. Worker and Consumer Risk Summary Tables (Tables 4-54 and 4-55) present benchmark values for dermal and inhalation exposure but oral exposure may also occur. The only reference to oral exposures in the draft risk evaluation occurs in 'footnote b' to Figure 1-3 – TCE Conceptual Model for Consumer Activities and Uses. Even though oral exposure is expected to be small, the risk evaluation should discuss why it is excluded.	As stated in the footnotes for Figure 1-5, mists of TCE will likely be rapidly absorbed in the respiratory tract or evaporate and not result in an oral exposure. Although less likely given the physical-chemical properties, oral exposure may also occur from incidental ingestion of residue on hand/body. Because oral exposure would be a very minor pathway relative to dermal and inhalation exposure, evaluation of risks via those routes is protective of any potential lesser risk from oral exposure.
SACC	**SACC COMMENTS:** Recommendation: Explain why risk characterizations for ONUs are	The "upper limit" notation indicated that the

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	appropriately identified as high-end exposures despite being based on central tendency exposure levels of workers. In Table 4-54, ONU exposures are estimated based on workers' central tendency exposure estimates, which are assumed to represent the high end of potential exposures to ONUs. The notation under the Population column for these ONUs is labeled as "upper limit." This notation is consistent with the expectation that ONU's exposures would be lower than the workers' exposures. Thus, it would be expected that these ONU exposure estimates correspond to the expected high end, not the central tendency (*i.e.,* they are derived from the central tendency estimate for the worker, but they represent the high-end exposure for the ONU).	ONU risk estimate was not based on actual data but was an extrapolation from worker central tendency values, which are expected to serve as a reasonable surrogate for upper-limit ONU exposure. To improve clarity the notation has been modified from "upper limit" to "worker estimate."
90	**PUBLIC COMMENTS:** Pushing through this draft risk evaluation in an expedited fashion would be a disservice to the American people and a violation of EPA's mandate to protect human health. This draft risk evaluation seems to prioritize boosting the use/sale of TCE regardless of personal risks to affected populations. We hope that EPA will abandon this expedited and incomplete analysis in favor of a comprehensive risk evaluation that meets the requirements of TSCA and provides what the public deserves.	EPA is finalizing the risk evaluation in a manner consistent with statutory and regulatory requirements and deadlines. Consistent with TSCA, EPA has evaluated unreasonable risk without consideration of costs or other non-risk factors.
108	**PUBLIC COMMENTS:** TSCA's standard requires EPA to resolve risks without consideration of costs or other non-risk factors. Other EPA-administered statutes allow consideration of non-risk factors and do not explicitly require consideration of vulnerable subpopulations. EPA cannot assume that regulatory efforts that meet the standards of these statutes also meet TSCA's requirement to eliminate unreasonable risks to PESS.	Per the statute (see TSCA section 6(b)(4)(A)) and the implementing regulations for risk evaluations (40 CFR part 702, subpart B), during risk evaluation, EPA must determine whether the chemical substance presents an unreasonable risk under its conditions of use. Upon finding unreasonable risk, EPA will apply risk management actions to the extent necessary so that the chemical no longer presents such risk, in accordance with TSCA section 6(a). In Section 2.3.3, EPA addresses the potentially exposed or susceptible subpopulations identified

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		as relevant based on greater exposure. EPA addresses the subpopulations identified as relevant based on greater susceptibility in Section 3.2.5.2. In developing the draft risk evaluation, the EPA analyzed the reasonably available information to ascertain whether some human receptor groups may have greater exposure than the general population to the hazard posed by TCE. EPA believes that coordinated action on exposure pathways and risks addressed by other EPA-administered statutes and regulatory programs is consistent with statutory text and legislative history, particularly as they pertain to TSCA's function as a "gap-filling" statute, and also furthers EPA aims to efficiently use Agency resources, avoid duplicating efforts taken pursuant to other Agency programs, and meet the statutory deadline for completing risk evaluations.
Ecological risk characterization		
SACC	**SACC COMMENTS:** Several committee members were concerned that overall environmental risks were not determined; only risks from TCE released to surface water and only risks posed to aquatic organisms were assessed. This limitation should be clearly restated in the risk characterization section.	In the draft risk evaluation, sediment-dwelling species were assessed qualitatively. However, in response to SACC comments a quantitative assessment of sediment organisms was added to the TCE risk evaluation in Section 4.1.3. For the terrestrial pathway, the environmental exposure pathways covered under the jurisdiction of other EPA-administered statutes and regulatory programs are not within the scope of

		the risk evaluation. Emissions to ambient air from commercial and industrial stationary sources, and associated inhalation exposures of terrestrial species, are under the jurisdiction of the Clean Air Act (CAA). Clarifying language about what pathways are addressed under other statutes has been added to Section 1.4.2 of the Risk Evaluation. During problem formulation EPA determined risks would not be evaluated for land-applied biosolids because based on fate properties, TCE is not anticipated to partition to biosolids during wastewater treatment. Any TCE present in the water portion of biosolids following wastewater treatment and land application would be expected to rapidly volatilize into air. In addition, TCE is not expected to bioaccumulate in tissues, and concentrations will not increase from prey to predator in either aquatic or terrestrial food webs. Lastly, based on the Guidance for Ecological Soil Screening Levels (EPA, 2003a, b) document, for terrestrial wildlife, relative exposures associated with inhalation and dermal exposure pathways are insignificant, even for volatile substances, compared to direct ingestion and ingestion of food (by approximately 1,000-fold). EPA has added language to the final risk evaluation document in Section 4.1.4 explaining this rationale.
SACC	**SACC COMMENTS:**	

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	Recommendation: Ensure environmental risk characterization statements are consistent with limitations imposed on the environmental risk assessment. Conclusions on environmental risk cannot consistently represent releases from >6000 facilities due to insufficient data; therefore, the evaluation cannot conclude that there are no risks to aquatic organisms. The draft risk evaluation underestimates TCE releases by a factor of 1.5 to 130, depending on multiple assumptions. Some facilities and species have an estimated RQ>1, but this is not translated in the risk determination or linked to a mode of use.	EPA modified the language in the risk characterization and conclusion section to read "EPA did not identify risks" where RQs were <1 or chronic and algae RQs were greater than or equal to 1 and? days of exceedance were less than 20 days.
SACC	**SACC COMMENTS:** Recommendation: Report the fraction of estimated TCE releases captured by monitoring data and improve the discussion of how total release time is determined. The Committee understands the modeling process used to determine days of exceedance from commercial uses (Appendix C) but was unable to follow the analysis that produced the days of exceedance. There are many instances in which the 7Q10 surface water concentration (SWC) exceeds the COC. If the mean SWC exceeds the COC, a description is required to demonstrate how fewer than 50% of the release days exceed the benchmark. If the explanation hinges on a log-normal distribution skewed toward higher concentrations, a quantitative verification is needed that none of the modeled concentrations exceed the acute toxicity COC.	The comment is unclear as to what the submitter defines as "monitoring data." Releases to water for all OES were based on TRI and DMR data where available. The assumptions and methodology used to estimate release days for each OES is described in Section 2.2.2.3. The uncertainties with these assumptions are described in Section 2.2.2.3. The E-FAST documentation manual provides more details on how the days of exceedance are estimated (U.S. EPA, 2007). E-FAST's PDM uses probability distributions as inputs to reflect that streams follow a highly variable seasonal flow pattern and there are numerous variables in a manufacturing process that can affect the chemical concentration and flow rate of the effluent.
SACC	**SACC COMMENTS:** Recommendation: Improve the justification for not assessing ambient air emissions and impacts from commercial and stationary sources. • It is concerning that these sources were excluded on a statutory basis, even though it is expected that most TCE will be removed in	For the terrestrial pathway, the environmental exposure pathways covered under the jurisdiction of other EPA-administered statutes and regulatory programs are not within the scope of

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	wastewater treatment by volatilization during aeration. It is not appropriate to assume ambient exposure risks are managed by the CAA. • EPA did not quantitatively assess exposure to sediment organisms because TCE is not expected to partition to sediment. Section 4.1.4 concludes that "physical-chemical properties do not support an exposure pathway through water and soil pathways to terrestrial organisms." However, Section 4.1.4 does not consider that soil invertebrates and burrowing mammals in functionally confined spaces may be exposed to TCE through vapor intrusion from contaminated underground water.	the risk evaluation. Emissions to ambient air from commercial and industrial stationary sources, and associated inhalation exposures of terrestrial species, are under the jurisdiction of the Clean Air Act (CAA). Clarifying language about what pathways are addressed under other statutes has been added to Section 1.4.2 of the Risk Evaluation. As explained in more detail in Section 1.4.2 of the Final Risk Evaluation, EPA believes it is both reasonable and prudent to tailor TSCA Risk Evaluations when other EPA offices have expertise and experience to address specific environmental media, rather than attempt to evaluate and regulate potential exposures and risks from those media under TSCA. EPA believes that coordinated action on exposure pathways and risks addressed by other EPA-administered statutes and regulatory programs is consistent with statutory text and legislative history, particularly as they pertain to TSCA's function as a "gap-filling" statute, and also furthers EPA aims to efficiently use Agency resources, avoid duplicating efforts taken pursuant to other Agency programs, and meet the statutory deadline for completing Risk Evaluations. EPA has therefore tailored the scope of the Risk Evaluation for TCE using authorities in TSCA Sections 6(b) and 9(b)(1).
SACC	**SACC COMMENTS:** Recommendation: Add worst-case scenarios from wastewater contaminated streams and add data on environmental vertebrate receptors for reproductive and developmental effects. Because hazard is identified but risk characterization is not conducted	EPA used the best available science and the reasonably available information during the data integration process. Hazard data did include developmental effects observed in amphibians.

	for aquatic receptors, additional discussion regarding uncertainty is warranted. "Worst-case scenarios" are missing from the Risk Characterization section. From the exposure aspect of the RQ evaluation, monitoring data from NPDES should be used to represent a "worst-case" exposure, particularly in wastewater dominated streams. From the effects/hazard side of the risk equation, data are absent for vertebrate reproduction and development in aquatic vertebrates.	Additionally, EPA considered surface water concentrations in receiving water bodies from wastewater treatment plants (WWTPs) based on TRI indirect release estimates or DMR reporting.
56, 74, 108	**PUBLIC COMMENTS:** • EPA identified unreasonable risk to aquatic organisms using RQs and dismissed this risk owing to uncertainty and relying on a dubiously calculated COC for algae. This approach is arbitrary and capricious because EPA refuses to accept the outcomes of its own analyses and conclusions run contrary to the evidence. Based on the analysis presented, EPA should find an unreasonable risk to the environment presented by certain COUs. • EPA identified risks (*e.g.,* to the most sensitive species of algae) but did not make risk findings. Unreasonable risk for some COUs were dismissed based on "uncertainties in the data" and on selective monitoring data that exclude contaminated environments and ranged across 5 orders of magnitude. • Uncertainties in the dataset were not explicitly specified. Uncertainty increases the chances of unreasonable risk. Uncertainty does not justify a finding of no unreasonable risk when EPA's own analysis supports a finding of unreasonable risk.	EPA had more confidence in the probabilistic approach used to derive the COC from the SSDs, and the SACC generally agreed with EPA's approach for algae. The SACC suggested using a higher assessment factor, and EPA agreed. From draft to final version of the TCE Risk Evaluation EPA changed the assessment factor from 1 to 5 to account for the uncertainties around using EC_{50}s rather than ChVs. If sufficient ChVs had been available EPA would have used them instead of EC_{50}s. This change has been made in Section 3.1.5. EPA considers the uncertainties associated with each condition of use, and how the uncertainties may result in a risk estimate that overestimates or underestimates the risk. Based on such analysis, EPA determines whether or not the identified risks are unreasonable.
56, 108	**PUBLIC COMMENTS:** Although EPA's analysis showed that TCE presents an unreasonable risk to aquatic organisms (based on releases from certain disposal and recycling facilities generating surface water concentrations above the COC for TCE), the analysis underestimated this risk, especially for algae. EPA's calculation of a COC for algae used SSD; algae "as a	EPA had more confidence in the probabilistic approach used to derive the COC from the SSDs, and the SACC generally agreed with EPA's approach for algae. The SACC suggested using a higher assessment factor, and EPA agreed. From

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	whole" were represented by nine species. EPA should use the most sensitive species as its indicator organism to develop protective COCs.	draft to final version of the TCE Risk Evaluation EPA changed the assessment factor from 1 to 5 to account for the uncertainties around using EC_{50}s rather than ChVs. If sufficient ChVs had been available EPA would have used them instead of EC_{50}s. This change has been made in Section 3.1.5.
65	**PUBLIC COMMENTS:** The draft risk evaluation demonstrates unreasonable risk to aquatic organisms, yet EPA dismisses unreasonable risk by invoking uncertainty.	EPA considers the uncertainties associated with each condition of use, and how the uncertainties may result in a risk estimate that overestimates or underestimates the risk. Based on such analysis, EPA determines whether or not the identified risks are unreasonable.
108	**PUBLIC COMMENTS:** The use of assessment factors in the development of COCs cannot be construed as "safety factors" that yield conservative estimates. In evaluating risks, EPA should recognize that assessment factors ensure greater accuracy rather than rendering the evaluation conservative.	EPA is in the process of evaluating the body of reasonably available literature on the subject in order to determine whether to revise standards for application of AF and the acute to chronic ratio for the next 20 high-priority substances undergoing risk evaluation. Until the body of scientific evidence for assessment factors is evaluated, EPA will continue to use OPPT methodology as cited in the risk evaluation (U.S. EPA 2013, 2012c) and apply an AF of 5 for acute and 10 for chronic aquatic invertebrate data. EPA considers these AFs to be protective of aquatic invertebrates from acute and chronic exposures to neutral organic substances such as TCE, which produce toxicity from simple narcosis.
Risk management/mitigation (including proposed ban)		
38	**PUBLIC COMMENTS:**	

	Request that rules for use and regulation of TCE not be relaxed from the TCE ban. Safer, alternative engineered solvents are available as cleaning fluids for manufacturing applications (*e.g.,* cleaning post soldering and ionic residues from electronic assemblies). TCE should not be used or sold without regulation and formal instructions for handling and disposal.	Per the statute (see TSCA section 6(b)(4)(A)) and the implementing regulations for risk evaluations (40 CFR part 702, subpart B), during risk evaluation, EPA must determine whether the chemical substance presents an unreasonable risk under its conditions of use. Upon finding unreasonable risk, EPA will apply risk management actions to the extent necessary so that the chemical no longer presents such risk, in accordance with TSCA section 6(a).
47	**PUBLIC COMMENTS:** In EPA's 2014 TCE TSCA Work Plan Risk Assessment, risks were assessed for its use in large/small commercial operations and consumer solvent degreasing, consumer use as a spray-applied protective coating for arts and crafts, and commercial use as a spot remover at dry cleaning facilities. This risk assessment was used to support two proposed rules under TSCA § 6 (81 FR 91592; December 12, 2016; 82 FR 7432; January 19, 2017) to ban these uses of TCE: • Notice in December 2016 to prohibit TCE's manufacture, processing, and distribution in commerce for use in aerosol degreasing and spot cleaning at dry cleaning facilities. • Notice in January 2017 to prohibit TCE's manufacture (including import), processing, and distribution in commerce for use in vapor degreasing, prohibit use of TCE in vapor degreasing. • Both notices also required downstream notifications of prohibitions throughout the supply chain and some form of limited recordkeeping. After the change in administration, both proposals were withdrawn, and no risk mitigation was implemented. The updated risk evaluation identified unreasonable risk for workers (and in most cases, ONUs) for every commercial COU. Unreasonable risk was identified for all but one consumer COU, and for the vast majority of uses, to bystanders. All but one trivial COU has been shown to pose a danger to the public health. It is time to proceed directly to rulemaking with a proposal to ban all further import, manufacture, and distribution of TCE for commercial and consumer uses in the U.S., followed by promulgation of the ban on all uses on an expedited timeline.	

108	**PUBLIC COMMENTS:** EPA proposed to ban the use of TCE in aerosol degreasing and spot cleaning in dry cleaning facilities in 2016 and vapor degreasing in 2017 owing to excessive risks to workers, bystanders, and/or consumers. • EPA's 2014 TCE Work Plan risk assessment and supplemental technical reports (based on peer review, best science available, and WOE) indicated that these uses present an unreasonable risk. • EPA's decision to re-evaluate risks associated with these uses was unnecessary and inappropriate. This action will delay or deny critical actions to protect workers and consumers. EPA should promptly act to finalize these bans even as it proceeds to finalize its risk evaluation focusing on risks from other COUs and exposures that would remain after banning these COUs.	
49	**PUBLIC COMMENTS:** It is critical for EPA to fully account for all TCE pathways of exposure and COUs, accurately and fully identify all health endpoints contributing to TCE's risks, and ensure that its risk evaluation and risk management actions protect vulnerable populations.	EPA thoroughly reviews all health endpoints associated with TCE in Section 3.2. Vulnerable populations are covered by accounting for PESS, as described in Sections 2.3.2.8, 3.2.5.2, and 4.4.1.
56	**PUBLIC COMMENTS:** EPA has contended that some issues discussed at previous SACC meetings were in the realm of policy and not relevant to SACC's charge, including EPA's decisions to: (1) exclude all general population risks from exposure releases to land, air, and water based on the assumption that this is addressed by other statutes; (2) assume that PPE is always used and effective; and (3) use a benchmark cancer risk level of $1x10^{-4}$ to define unreasonable risk to workers. EDF strongly disagrees that these issues are beyond the scope of the SACC. These decisions have major direct scientific consequences, as they clearly lead to underestimations of chemicals' risk to the environment, the general population, workers, and vulnerable subpopulations. In the Final SACC Reports for 1,4-dioxane, 1-bromopropane, and methylene chloride, the SACC appropriately addressed some of these issues and should	EPA considers all comments from the public and SACC when updating science policy determinations. Nevertheless, decisions such as benchmarks to use within established ranges and what pathways are in scope remain within the realm of EPA's policy decision-making authority.

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	continue doing so in future reports with a particular emphasis on how those determinations affect the scientific accuracy and legitimacy of the risk evaluations.	
56, 108	**PUBLIC COMMENTS:** TSCA divides risk evaluation and management processes so that regulatory measures are considered after determinations of unreasonable risk. EPA's choice to make risk determinations based on an assumption of PPE conflates risk evaluation and management, leading EPA to not find an unreasonable risk or to underestimate the extent and magnitude of these risks. EPA's failure to make unreasonable risk determinations could potentially deny itself the opportunity to impose mandatory requirements to control workplace exposures.	For the purpose of this Risk Evaluation, EPA makes assumptions about potential PPE use based on reasonably available information and expert judgment. EPA considers each condition of use and constructs exposure scenarios with and without engineering controls and /or PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. Again, while EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgment underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. Additionally, in consideration of the uncertainties and variabilities in PPE usage, including the duration of PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties.
81	**PUBLIC COMMENTS:** Are there any new legal obligations, so as, to assure safe and healthful	Per the statute (see TSCA section 6(b)(4)(A))

	living conditions {water consumption - in public} and working conditions by an approved state plan or standard regulations, to provide people with recognized hazards likely to cause death or serious physical harm. How valuable will the draft risk evaluation for TCE be if not legally supported? Will it be enough to help identify risk levels and to determine any appropriate control measures to implement?	and the implementing regulations for risk evaluations (40 CFR part 702, subpart B), during risk evaluation, EPA must determine whether the chemical substance presents unreasonable risk under its conditions of use. Upon finding unreasonable risk, EPA will apply risk management actions to the extent necessary so that the chemical no longer presents such risk, in accordance with TSCA section 6(a).
84	**PUBLIC COMMENTS:** TCE poses a high risk of exposure to the end-user of the chemical, is a suspected carcinogen, and has been detected in groundwater. Commercially available alternatives exist to replace TCE. Honeywell currently offers a better alternative to TCE for at least three uses, including vapor/immersion degreasing, aerosol cleaning, and adhesives.	EPA appreciates the information on the alternatives to TCE and will consider them during risk management.
86	**PUBLIC COMMENTS:** Major problems in the draft risk evaluation will result in families being left unprotected. We are very concerned that EPA's draft risk evaluation for TCE, if finalized without major improvements, will fail to protect public health. Our families and our communities are among those that have been significantly impacted by TCE; this process is not theoretical for us.	EPA has improved the final Risk Evaluation based on public and SACC comments. The Risk Evaluation for TCE evaluates all associated conditions of use. For any conditions of use where unreasonable risk was identified, EPA will proceed to risk management during which EPA will consider all available regulatory options.
88	**PUBLIC COMMENTS:** There is concern regarding EPA's decision to abandon the previously proposed bans on high-risk uses of TCE.	Regulatory actions to address unreasonable risks are outside the scope of this risk evaluation. EPA has decided to re-evaluate TCE uses from the proposed TSCA section 6(a) rules in order to assess them under the updated TSCA statute.
92	**PUBLIC COMMENTS:** The effort to replace the previous rule should be scrapped. Independent scientists agree that TCE is highly toxic, and that even trace amounts can damage developing hearts of human beings. The rule previously in place was founded on science responsible to data, not to chemical industry interests, and should remain in effect.	
Risk characterization other		

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SACC	**SACC COMMENTS:** Recommendation: Clearly and explicitly state in Section 4 the fundamental objective of the environmental or human health risk characterization. The following issues and questions need more emphasis: • What is the most sensitive endpoint for each exposure route and use, for both acute and chronic non-cancer effects and cancer? Also, explicitly define what is meant by "most sensitive." • Limitations and data gaps need to be presented in a more highlighted and obvious manner. • Areas of controversy should be highlighted.	Section 4.1 and 4.4.1 (for environmental risks) and 4.2.1 (for human health risks) describe the risk characterization process, which integrates exposure and hazard in order to determine whether there is risk for the chemical based on scientifically established benchmarks. Section 4.2.1.1 presents the endpoints used for risk estimates in the Risk Evaluation, including the most sensitive chronic POD for each hazard domain. Limitations, data gaps, and controversies are discussed throughout the Risk Evaluation in the "Assumptions and Key Sources of Uncertainty" sections.
Risk determination (unreasonable risk/no unreasonable risk)		
SACC	**SACC COMMENTS:** Recommendation: Clarify why Pepper Spray, given that its MOE is below the benchmark MOE, does not present an unreasonable risk. One Committee member noted that the results for Pepper Spray (Table 4-51) show that its MOEs for consumer users are below the benchmark MOE and also below the MOE for the congenital heart defects endpoint. This is an important point to include in the discussion because it is the only consumer COU that is found to not present an unreasonable risk to this higher (but controversial) benchmark.	While Pepper Spray does indicate risk for developmental neurotoxicity and congenital heart malformations, EPA has reduced confidence in the dose-response results for those studies (Fredriksson et al., 1993), (Johnson et al., 2003). Therefore, risk conclusions are based on the robust and sensitive acute immune endpoint from (Selgrade and Gilmour, 2010) which was the best overall acute endpoint based on the best available science and weight of scientific evidence.
56, 108	**PUBLIC COMMENTS:** EPA underestimates occupational risk leading to "no unreasonable risk" findings or understatements of the extent and magnitude of unreasonable risks. Occupational risks were underestimated by: • EPA's assumption that PPE will be used in most scenarios to avoid finding risk estimates represent unreasonable risk or to understate	For the purpose of this Risk Evaluation, EPA makes assumptions about potential PPE use based on reasonably available information and expert judgment. EPA considers each condition of use and constructs exposure scenarios with and

	the extent. • EPA finding cancer risk unreasonable only if it exceeds a level of 1 in 10,000, which is as much as 100 times higher a risk than warrants regulation under TSCA. For ONUs, EPA fails to identify unreasonable risks for the most highly exposed/most vulnerable based on risk determinations that relied exclusively on central tendency estimates of exposure.	without engineering controls and /or PPE that may be applicable to particular worker tasks on a case-specific basis for a given chemical. Again, while EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgment underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. Additionally, in consideration of the uncertainties and variabilities in PPE usage, including the duration of PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties. EPA, consistent with 2017 NIOSH guidance, used $1x10^{-4}$ as the benchmark for the purposes of this unreasonable risk determination for individuals in industrial and commercial work environments, including workers and ONUs. EPA has consistently applied a cancer risk benchmark of $1x10^{-4}$ for assessment of occupational scenarios under TSCA. $1x10^{-4}$ is not a bright line and EPA has discretion to make unreasonable risk determinations based on other

		benchmarks as appropriate. See Section 5.1.1.2 of the risk evaluation for additional information. Where EPA had monitoring or modeled data specific to ONUs, unreasonable risk determinations where made based on high-end exposures. For conditions of use where the data did not distinguish between worker and ONU inhalation exposures, there was uncertainty regarding ONU exposure. ONU inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation exposures when determining ONUs' unreasonable risk (rather than the high-end inhalation exposures), when data specific to ONUs was not available.
98	**PUBLIC COMMENTS:** Pursuant to TSCA Section 6(b), EPA must determine if TCE presents an unreasonable risk under the COUs as a single determination (rather than for each condition). EPA concluded that most COUs of TCE present an unreasonable risk. However, EPA needs to make an overall determination as to whether TCE presents an unreasonable risk. The evidence that EPA has already reviewed in its draft risk evaluation compels a finding of yes.	Per 40 CFR 702.47 "…EPA will determine whether the chemical substance presents an unreasonable risk of injury to health or the environment under each condition of use within the scope of the risk evaluation…." This approach in the implementing regulations for TSCA risk evaluations, is consistent with statutory text in TSCA section 6(b)(4)(A), which instructs EPA to conduct risk evaluations to determine whether a chemical substance presents an unreasonable risk "under the condition of use."
99	**PUBLIC COMMENTS:** EPA's determinations that individual COU of TCE pose no unreasonable risk violate TSCA. This "use-by-use" approach to risk determinations is unlawful and threatens to prevent EPA from eliminating the unreasonable risks posed by TCE. TSCA commands that EPA determine whether "a chemical substance" (not particular uses	

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	of a chemical substance) presents an unreasonable risk in a single, comprehensive determination. This holistic risk determination must reflect EPA's evaluation of all TCE's COUs considered in combination. EPA must revise its risk evaluation for TCE to make a single risk determination for the chemical substance. Based on EPA's findings that some COUs present unreasonable risks to health, EPA must conclude under TSCA section 6(b)(4)(A) that TCE presents an unreasonable risk to human health.	
102	**PUBLIC COMMENTS:** Under the Lautenberg Chemical Safety Act, a 'use' receives federal preemption only if it is included in the scope of the risk evaluation and if EPA makes a definitive determination as to risk. For this reason, it is critical that EPA clearly make determinations of unreasonable risk and no unreasonable risk. EPA made no determination related to general population risk (but rather relied on other statutes to manage exposure to the general population). We request that EPA clarify how regulation of "conditions of use" covered by other EPA statutes is considered adequate to meet the Lautenberg Chemical Safety Act finding of "no unreasonable risk" and preclude state preemption of EPA's findings. Similarly, we request that EPA articulate the legal argument as to how other COUs that EPA has determined are adequately regulated by other federal agencies cannot be preempted by states.	As explained in more detail in Section 1.4.2 of the Risk Evaluation, EPA believes it is both reasonable and prudent to tailor TSCA Risk Evaluations when other EPA offices have expertise and experience to address specific environmental media, rather than attempt to evaluate and regulate potential exposures and risks from those media under TSCA. EPA believes that coordinated action on exposure pathways and risks addressed by other EPA-administered statutes and regulatory programs is consistent with statutory text and legislative history, particularly as they pertain to TSCA's function as a "gap-filling" statute, and also furthers EPA aims to efficiently use Agency resources, avoid duplicating efforts taken pursuant to other Agency programs, and meet the statutory deadline for completing Risk Evaluations. EPA has therefore tailored the scope of the Risk Evaluation for TCE using authorities in TSCA Sections 6(b) and 9(b)(1). Under TSCA section 18(a)(1)(B) and (c)(3), federal preemption over certain State actions

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		applies to chemical substances for which a determination of 'no unreasonable risk' has been made pursuant to TSCA section 6(i)(1) or for which a final risk management rule is promulgated pursuant to TSCA section 6(a) and does not extend to those hazards, exposures, risks, and uses or conditions of use not included in that final determination or rule. Pursuant to TSCA section 18(c)(3), if uses or exposure pathways are not "included in any final action the Administrator takes pursuant to section [6(a) or 6(i)(1)]," (*e.g.,* because EPA determines the use or exposure pathway to be outside of the scope of the risk evaluation (such as uses or exposure pathways regulated by EPA or other Federal agencies under other federal laws)), then TSCA permanent preemption does not apply. As the commenter notes, EPA clearly stated in the risk evaluation for TCE that it did not evaluate exposures to the general population, and as such the unreasonable risk determinations for relevant conditions of use do not account for exposures to the general population. Thus, exposures to the general population are not included in any final determinations of 'no unreasonable risk' for TCE and TSCA preemption based on those 'no unreasonable risk' determinations does not apply to those exposures.
102	**PUBLIC COMMENTS:** The International Material Data System (IMDS) is used by many in the automotive sector as a first screen to identify potential uses of chemical substances. The IMDS has been adopted as the global standard for reporting material content throughout the automotive supply chain and	The request by the commenter is outside the scope of EPA's risk evaluation. This may be addressed during the risk management phase only for those conditions of use that present

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	for identifying which COCs to human health and the environment are present in finished materials and components. The threshold for reporting in this system is 0.1% by weight, a threshold that has been almost universally adopted by international regulatory bodies and many states within the United States. The presence of any chemical below this threshold is not required to be reported in IMDS based on a low underlying expected risk of exposure from de minimis quantities. We request that EPA identify a de minimis level for TCE and other TSCA chemicals below which EPA has no reasonable basis to conclude that there is an unreasonable risk.	unreasonable risk.
106	**PUBLIC COMMENTS:** EPA finds that TCE presents risks of concern for many COUs across workers, ONUs, consumers, and bystanders. However, we assert that critical scientific flaws in EPA's risk assessment approach led to underestimation of risk; the actual risks are of greater magnitude than that stated by EPA and additional COUs present unreasonable risks.	EPA has made determinations of unreasonable risk based on the best available science while considering high-end exposure estimates and sensitive and robust health endpoints.
108	**PUBLIC COMMENTS:** Deficiencies in the draft risk evaluation (including exclusion of known uses and exposures, insufficient consideration of susceptible populations, underestimation of occupational risks, dismissal of risk by invoking uncertainty, failure to adequately evaluate environmental risks of TCE release and exposure, and use of a flawed systematic review process) compromise risk determinations for individual COUs presented in Table 5-1 and Section 5.3 of the draft risk evaluation. • These factors lead to a systematic underestimation of risks from individual COUs, including risks to human health (specifically vulnerable populations) and the environment. • Flaws in the draft risk evaluation mean that EPA has clearly not provided support for any assertion that TCE, across all its COUs, does not present unreasonable risk. EPA's determinations that many COUs do present unreasonable risk supports the conclusion that the chemical as a whole presents unreasonable risk.	EPA makes determinations of unreasonable risk on a COU-basis, not for the chemical as a whole. EPA has performed a thorough risk evaluation covering all associated COUs based on the best available science including the results of systematic review. Unreasonable risk was found for all but two out of 54 COUs. Per 40 CFR 702.47 "…EPA will determine whether the chemical substance presents an unreasonable risk of injury to health or the environment under each condition of use within the scope of the risk evaluation…". This approach outlined in the implementing regulations for TSCA risk evaluations is consistent with the statutory text in TSCA section

108	**PUBLIC COMMENTS:** In violation of TSCA, EPA failed to consider if TCE "as a whole" (*i.e.,* all hazards, exposures, and COUs) presents an unreasonable risk. EPA should change the final risk evaluation to assess the reasonably available information on all hazards and exposures for TCE, and that information should inform EPA's evaluation of the risks of this chemical.	6(b)(4)(A), which instructs EPA to conduct risk evaluations to determine whether a chemical substance presents an unreasonable risk "under the conditions of use."
108	**PUBLIC COMMENTS:** The plain text, overall structure, purpose, and legislative history of TSCA indicate that EPA must determine whether a chemical substance presents an unreasonable risk comprehensively (*i.e.,* for the chemical as a whole). EPA is required under TSCA to consider all reasonably available information regarding hazards, exposures, and COUs, without limitation and without the discretion to ignore any of this information. Moreover, TSCA requires that EPA evaluate a chemical's risk without consideration of costs or other non-risk factors; by excluding certain hazards, exposures, or COUs, EPA is considering non-risk factors. The requirement to consider chemical substances as a whole expressly requires EPA to address risks when risks arise from combined sources of exposure. EPA must analyze all exposures and assess whether any combination presents an unreasonable risk. In addition, if the risk evaluation fails to address all hazards and exposures, it undermines the purpose of TSCA and the requirement that EPA rely on the best available science. Finally, the legislative history of TSCA requires EPA to integrate exposure and hazard information to assess risk.	
Selection of key endpoints for risk conclusions/determination		
SACC	**SACC COMMENTS:** Recommendation: Revise and expand the justification for not using fetal cardiac malformations as the unreasonable risk driver. • Exposure to TCE during pregnancy linked to heart defects is controversial, and the discussion in the draft risk evaluation does not resolve the topic. The Committee agreed that heart malformations could be used for hazard identification but was divided on the use of	EPA has expanded the justification for selection of the immune studies as the best overall endpoints. While congenital heart defects may be of concern to particular susceptible subpopulations, the inconsistency of the data suggests that it is not the best overall endpoint for

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	this endpoint for risk characterization. The risk evaluation needs to better discuss the rationale for excluding fetal heart malformations given that the 2011 IRIS evaluation computed a POD for this endpoint. • The Committee also noticed a disconnect between the extensive discussion of fetal heart malformation data and the controversy surrounding these findings. The draft risk evaluation presents a dose-response analysis of the data but ultimately dismisses it in favor of the immunosuppression POD. Some Committee members felt that the risk evaluation should better explain why fetal cardiac malformation data are not used as the unreasonable risk driver. It appeared to some Committee members that basing unreasonable risks on immunosuppression rather than fetal heart malformations is an acceptance of less protective concentration levels.	TCE toxicity overall. EPA acknowledges that while there is qualitative support for the endpoint, based on uncertainties in the dose-response for this endpoint and other considerations EPA has selected immune endpoints as the best overall endpoints for risk conclusions (Sections 3.2.5.4.1, 3.2.6.1.1). Additionally, EPA has expanded discussion of the history of Johnson et al, 2003 and the cardiac defects endpoint in Appendix F.1. EPA has moved a significant portion of the detailed discussion on cardiac malformations to Appendix F in order to avoid too heavily focusing on an endpoint other than the best overall ones in the main body.
SACC	**<u>SACC COMMENTS:</u>** Recommendation: Improve the justification for immunosuppression over congenital heart defects as the unreasonable risk driver for acute non-cancer risks. • Outside parties claimed that an early version of the draft risk evaluation identified fetal cardiac effects as the most sensitive endpoint/risk driver (consistent with prior TCE reviews) but that non-scientific pressures caused EPA to shift to immune findings. • Both endpoints are discussed in the hazard section. Although some justification is provided for the selection of immunosuppression as the risk driver, the rationale for this decision (different than that used in the 2011 IRIS evaluation) should be further discussed. • Greater transparency is warranted in the rationale for selection of the "best" representative sensitive responses. Some Committee members would like an explanation as to whether the decision to use immunosuppression over congenital heart defects was based on uncertainty. There is a disconnect between the decision to exclude congenital heart defect data and the amount of text given to support the decision to use these data in earlier sections.	EPA routinely conducts Inter-Agency review of its TSCA Risk Evaluation before SACC peer review and public comments. Federal experts in toxicology, epidemiology, and industrial hygiene among other disciplines help EPA develop more comprehensive and rigorous risk evaluations. In this particular Inter-Agency review EPA discussed, among other things, the strengths and weaknesses associated with use of the cardiac defects endpoint as the basis of the risk conclusions. Based on these discussions, EPA concluded that whereas evidence indicates that CHDs may be of concern for susceptible subpopulations, the inconsistency of the data and reduced confidence in dose response results suggest that it is not the best indicator of TCE toxicity overall. For purposes of risk evaluations under TSCA, EPA chose to use immune

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	• The draft risk evaluation presents human health risk conclusions based on key studies in Tables 4-55 and 4-56, including derivations based on the Johnson data. Some Committee members suggest not including heart defect risk values in these tables to allow focus on the immunosuppression risk.	endpoints as the indicator of TCE toxicity based on their consistency, reduced uncertainty, and robustness of the data.
SACC	**SACC COMMENTS:** Some Committee members called for this draft risk evaluation to consider and discuss differences between health effect values derived from this risk evaluation with those derived and/or used by other EPA regulatory programs, federal regulatory agencies, and non-federal entities. The discussion could provide support for the new TSCA health effect levels or for more protective levels currently established under other programs. EPA should consider adding information about the key drivers in the setting of other exposure guidelines to provide context and improve understanding of the various occupational/consumer/public exposure mandates and guidelines.	EPA indicates throughout Section 3.2 where the Risk Evaluation differs and agrees with previous assessments by EPA and other organizations. Notably, the updated TSCA statute has different requirements and considerations than the old law or other EPA statutes, and therefore "protective levels" should not be directly compared across assessments.
SACC	**SACC COMMENTS:** One Committee member suggested that approaching the setting of health effect levels more in the manner of a meta-analysis might provide a more robust approach than basing the value on a single study and a most sensitive endpoint. This approach might provide a firmer foundation on which to base future risk management decisions.	TSCA considers both best available science and protection of PESS groups in selecting PODs to use for risk estimation. Based on these considerations, EPA utilizes PODs representing the most sensitive endpoints from among the most robust and well-supported studies.
SACC	**SACC COMMENTS:** The draft risk evaluation identifies many COUs that pose unreasonable risk. These conclusions follow estimated risks exceeding the MOE for particularly sensitive endpoints that some Committee members consider outliers, and which are the focus of controversy. Consequently, the derived occupational exposure levels are orders of magnitude below those currently used to protect workers by industrial hygienists (*e.g.,* ACGIH Threshold Limit Values [TLVs], time weighted averages; NIOSH RELs, and OSHA PELs).	EPA agrees that many of these occupational exposure thresholds (*e.g.,* TLVs, OSHA PELs) are above exposure levels that would be protective of risks identified in this Risk Evaluation.
36	**PUBLIC COMMENTS:**	

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	The draft risk evaluation changes the method of the assessment, from levels that will cause abnormalities in fetal cardiac tissue to the levels of TCE found to trigger no immunosuppression. Given that the study used in the current draft risk evaluation uses an exposure level 500 times higher than the exposure found to trigger heart defect in the Johnson et al. (2003) study, this information needs careful consideration. It may potentially impact on the future children of the United States.	EPA has expanded the justification for selection of the immune studies as the best overall endpoints. EPA believes these endpoints represent the "best available science" based on the weight of scientific evidence in accordance with TSCA and the use of these endpoints for risk conclusions was supported by SACC peer reviewers (https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0500-0111). TSCA requires EPA to select exposure and hazard values based on the best available science, not simply the lowest values. EPA routinely conducts Inter-Agency review of its TSCA Risk Evaluation before SACC peer review and public comments. Federal experts in toxicology, epidemiology, and industrial hygiene among other disciplines help EPA develop more comprehensive and rigorous risk evaluations. In this particular Inter-Agency review EPA discussed, among other things, the strengths and weaknesses associated with use of the cardiac defects endpoint as the basis of the risk conclusions. Based on these discussions, EPA concluded that whereas evidence indicates that CHDs may be of concern for susceptible subpopulations, the inconsistency of the data and reduced confidence in dose response results suggest that it is not the best indicator of TCE toxicity overall. For purposes of risk evaluations under TSCA, EPA chose to use immune endpoints as the indicator of TCE toxicity based
37	**PUBLIC COMMENTS:** Extensive revisions were made to EPA's draft risk evaluation of TCE during the interagency review process. The draft provided for interagency review identified fetal cardiac malformations as the most sensitive endpoint and used it to derive the PODs for making determinations of risk. The draft released to the public and provided to the SACC for peer review significantly downgrades this endpoint and bases its risk determinations of acute and chronic risks on immune endpoints. The implications are significant as evident from the orders-of-magnitude differences in the MOEs calculated for fetal cardiac effects versus the selected immune endpoints and given the differing subpopulations at risk. It is essential that EPA make available the draft of the risk evaluation prior to the revisions that was submitted for interagency review. Additionally, EPA must provide a complete explanation of the basis for the revisions. Absent this information, the SACC's ability to peer-review the draft TCE risk evaluation will be significantly impaired.	
47	**PUBLIC COMMENTS:** As articulated in the draft risk evaluation, it appears that EPA is using a new and unvetted policy to select the most "representative" (rather than the most sensitive) endpoint, which is at odds with long-standing agency-wide risk assessment practices. The Environmental Protection Network (EPN) is deeply concerned about this new policy, which provides EPA with the discretion to ignore the most sensitive endpoint. On p. 257, EPA documents how this policy was used to select a less sensitive endpoint than congenital heart defects as the basis for acute	

	and chronic non-cancer PODs. A few factors of this policy were used to justify the selection of immune endpoints for acute and chronic effects, but congenital heart defects were not evaluated based on the same factors. It is critically important that EPA not replace the protective health policy of selecting the most sensitive endpoint with this "representative policy." There is no scientific justification for this new policy, which could have a wide range of effects, undermining the reference doses and cancer potency factors developed for all chemicals.	on their consistency, reduced uncertainty, and robustness of the data. EPA has created a new subsection identifying and justifying the two immune endpoints as best overall of risk conclusions (Section 3.2.5.4.1). EPA's conclusions are based on the best available science and weight of scientific evidence. EPA used the best overall endpoints as the basis of risk conclusions (Section 4.5) and unreasonable risk determinations (Section 5.2). The draft risk evaluation underwent numerous rounds of revisions both from internal and external reviewers throughout the development of the published draft. The development of the draft risk evaluation is an ongoing deliberative process and EPA is not obligated to provide descriptions of predecisional and deliberative discussions or consultations with other federal agencies. In the interest of continuing to have open and candid discussions with our interagency partners, and as a matter of policy, EPA does not publicly release internal deliberative drafts or intend to include the content of those discussions in the risk evaluation. It is unclear whether the totality of the scientific database examining immune-related endpoints is larger or smaller than the database for cardiac effects, however the database for immune-related endpoints is certainly more consistent. Indications of both immunosuppression and autoimmunity were consistently observed in
47, 73, 74, 108	**PUBLIC COMMENTS:** The initial draft risk evaluation relied on fetal heart defects as the most sensitive endpoint. Outside parties allegedly forced EPA career staff to make fundamental changes to the draft risk evaluation before it was released to the public and presented to SACC for peer review; namely, a change in the key health endpoint for risk determinations from congenital heart defects to immune endpoints. The notion of political interference was initially uncovered by Elizabeth Shogren of the Center for Investigative Reporting and was also noted by a member of the peer review panel at the TCE SACC meeting. This sorry episode heavily taints the scientific integrity and credibility of EPA's draft risk evaluation. The decision not to rely on congenital heart defects for EPA's determinations of TCE's acute and chronic risks deviates from scientific best practices, defies requirements under the law, and is not sufficiently protective of public health, particularly the health of especially vulnerable subpopulations.	
49, 99	**PUBLIC COMMENTS:** In the past (including EPA's 2011 IRIS and 2014 Workplan assessments), EPA consistently concluded that the weight of scientific evidence supports the link between TCE and fetal heart malformations, and as the most sensitive endpoint, should be used to drive risk determinations for acute and chronic exposures. This formed the basis of the proposal in 2016/2017 to ban vapor and aerosol degreasing and spot removal uses of TCE under TSCA. The original draft risk evaluation (December 2019) used the study by Johnson et al. (2003) for	

	determination of MOEs for TCE workers and consumers; however, investigative reporting (by Elizabeth Shogren) indicates that outside parties allegedly directed EPA not to use this endpoint (based on uncertainty and decreased confidence in the endpoint) but rather use immune-related endpoints. The revised draft suggests that exclusion of heart defects is inconsequential from a health perspective because unreasonable risk determinations remain the same for most COUs. This is misleading because immune effects occur at significantly higher dose levels than heart malformations. For example, the acute HEC99 based on immune effects is 470 times higher than that for heart malformations, resulting in MOEs that are two orders of magnitude higher than for heart defects. Therefore, exposure limits based on immune effects expose women to TCE levels that would leave their offspring at risk for heart malformations. There is no scientific justification for this decision. • EPA repeatedly finds that the WOE demonstrates that TCE causes heart malformations, and data are sufficient for dose-response analysis and subsequent risk determinations. • The only change since the earlier assessments is a study by the HSIA, which indicated that TCE does not cause heart malformations. However, the risk draft evaluation notes that methods were less sensitive, a full range cardiac effects were not examined, and a dose-related increase on heart malformations was observed. • The selection of immune effects as a representative endpoint should drive risk determinations at the exclusion of other more sensitive endpoints. The choice of this endpoint over heart defects based on confidence violates long-standing public health policy to protect against the most sensitive health endpoints. The implication that data supporting immune effects are more 'certain' than evidence for heart defects is an invention of outside parties with no support elsewhere in the draft risk evaluation.	epidemiological and animal studies, in both adults and developmental contexts, and in both normal and autoimmune-prone rodents (Sections 3.2.3.1.4 and 3.2.3.1.6. In contrast, cardiac effects are supported mechanistically however epidemiological support is strong only for select subpopulations and the animal database (which would be most suitable for dose-response) provides overall ambiguous conclusions (Appendix F.3). From the EPA Guidelines for Developmental Toxicity Risk Assessment: "the hazard identification/ dose-response evaluation and the exposure assessment for given populations are combined to estimate some measure of the risk for developmental toxicity. As part of risk characterization, a summary of the strengths and weaknesses in each component of the risk assessment is discussed along with major assumptions, scientific judgments, and, to the extent possible, qualitative and quantitative estimates of the uncertainties. The Guidance does describe using the most sensitive effect for deriving the RfD, however TSCA does not use RfDs for risk characterization. EPA under TSCA uses an MOE approach instead of a hazard index/reference concentration approach because benchmarks for cancer and non-cancer risk estimates are not bright lines, and EPA has discretion to make unreasonable risk determinations based on other risk benchmarks or factors as appropriate. The RfC defines an
49, 99	**PUBLIC COMMENTS:**	

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	The revised risk evaluation indicated that while congenital heart defects were identified as the most sensitive endpoint, there were uncertainties that decreased confidence on this endpoint. • These uncertainties and the rationale for decreased confidence in the endpoint were not further discussed. • Based on EPA's "weight of the scientific evidence" for this endpoint, EPA indicated that TCE-related cardiac effects in animals was 'independently verified' in epidemiology and mechanistic studies, the database was reliable, and that it provided positive evidence that TCE may cause heart defects in humans. • Based on EPA's evaluation of the "best available science," the key study used for dose-response analysis (Johnson et al., 2003) was scored medium, and therefore acceptable for inclusion in the risk evaluation. • EPA reached the same conclusions on the validity of the heart defects endpoint in 4 separate assessments that have been reviewed by the SAB and NAS. This draft disavows a decade of scientific work based on 'uncertainty;' this is the opposite of the "best available science" EPA is obligated to use under TSCA. To achieve this, outside parties allegedly directed EPA to apply the novel approach of selecting a "representative endpoint" to determine unreasonable risk; ignoring more sensitive endpoints that present greater risk. This approach is without precedent, is not health-protective, and would be contrary to EPA's obligation to determine whether TCE presents an unreasonable risk to a potentially exposed or susceptible subpopulation.	exposure that is "likely to be without an appreciable risk of deleterious effects during a lifetime." In contrast, TSCA uses unreasonable risk determinations that incorporate many considerations and the risk evaluation does not set a goal of determining an all-encompassing "safe" exposure level. EPA does consider risks to infants and children and presents risk estimates for multiple developmental endpoints, however the basis for unreasonable risk determinations are different than the basis for establishing an RfD/RfC. As explained in the preamble to the Risk Evaluation Rule, "to make a risk determination, EPA may weigh a variety of factors in determining unreasonable risk. The Administrator will consider relevant factors including, but not limited to: The effects of the chemical substance on health and human exposure to such substance under the conditions of use (including cancer and non-cancer risks); the effects of the chemical substance on the environment and environmental exposure under the conditions of use; the population exposed (including any susceptible populations), the severity of hazard (the nature of the hazard, the irreversibility of hazard), and uncertainties." 82 FR at 33735.
56, 108	**PUBLIC COMMENTS:** EPA based its determinations of acute and chronic unreasonable risk on immune-related endpoints rather than fetal cardiac defects. This decision is counter to the preponderance of scientific evidence that TCE induces fetal cardiac malformations and reflects an agency choice at odds with scientific policy and practice, statutory requirements to protect potentially exposed and susceptible subpopulations, and the	

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	mission of protecting human health.	
56, 108	**PUBLIC COMMENTS:** EPA's rationale for making risk determinations based on immune-related endpoints raises significant concerns. The decision to use "mortality due to immunosuppression" as the selected acute noncancer endpoint (Selgrade and Gilmour, 2010) and "autoimmunity" as the chronic non-cancer endpoint (Keil et al., 2009) was based on its rating of these studies as "High" quality per the TSCA systematic review method, whereas EPA rated the Johnson (2003) study, used in previous EPA assessments to derive a point of departure, as "Medium." This scientifically unsupported and contradictory decision results in EPA relying its risk determinations on risk estimates across various TCE exposure scenarios that are orders of magnitude more lenient than those risks estimates associated with the most sensitive endpoint, fetal cardiac malformations.	
56, 108	**PUBLIC COMMENTS:** Although EPA recognizes that developmental studies are relevant for evaluating acute exposure scenarios, EPA chose to rely its MOE values based on immunosuppression. This decision is flawed and contradicts long-standing policy and previous EPA assessments of TCE that require basing risk assessment and protection on the most sensitive endpoint. Previous assessments (EPA 2014 TCE work plan assessment and TSCA section 6 proposed rules for the use of TCE in vapor degreasing, and in spot cleaning and dry cleaning facilities) relied on developmental endpoints for assessing the health risks of TCE from acute exposure.	
56, 108	**PUBLIC COMMENTS:** EPA's decision not to take a health-protective approach to assessing acute TCE risks is at odds with TSCA's requirement to protect potentially exposed or susceptible populations, which explicitly includes pregnant women and children. • TSCA's requirement that EPA assess risks to susceptible populations demands that EPA base its risk determinations on the endpoint (congenital heart defects) that specifically impacts	

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	pregnant women, infants, and children. • EPA acknowledges that congenital heart defects were the most sensitive endpoint, and this endpoint is relevant to potentially exposed or susceptible populations of pregnant women, infants, and children, and instead relies on a far less sensitive endpoint not relevant to those subpopulations for its risk determinations. This decision results in EPA making risk determinations based on a more lenient benchmark and failing to carry out its mandate under TSCA 6(b)(4)(A). EPA cannot adequately protect against risks specific to pregnant women (and their developing fetuses), infants, or children by selecting immune effects as the basis for its determinations. EPA must develop risk determinations that address the endpoint (congenital health defects) that specifically impacts this subpopulation.	
56, 108	**PUBLIC COMMENTS:** EPA's decision to make risk determinations based on immune-related endpoints represents a break with decades of agency scientific policy and practice designed to protect human health. EPA's determinations of unreasonable risks based on immune endpoints results in a significantly higher POD (*e.g.,* based on Selgrade and Gilmour, 2010), indicating that the selected endpoint is orders of magnitude less sensitive than the congenital heart defects endpoint. With this decision, EPA has chosen not to protect against the most sensitive endpoint, for which there is strong scientific support. The overall database for immune-related endpoints is far more limited than the congenital heart defects endpoint, and this endpoint is less sensitive and not subjected to the same WOE analysis to which the congenital heart defects data were subjected.	
56, 74, 108	**PUBLIC COMMENTS:** In defiance of public health protection and statutory requirements under TSCA to protect PESS, EPA chose immune effects as its basis for risk determinations rather than fetal cardiac malformations. EPA indicated that the choice was based on the highest quality information for which EPA has the greatest confidence. EPA's decision to ignore strong scientific evidence that TCE induces fetal cardiac malformations at	

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	levels of exposure lower than immune-related effects is scientifically unsupported and contrary to EPA's mission to protect health and to protect a critical susceptible subpopulation (pregnant women and the developing fetus). EPA's choice also contradicts previous assessments of TCE and existing EPA guidance to protect sensitive subpopulations and to protect against the most sensitive endpoint, including: • EPA's Guidelines for Developmental Toxicity Risk Assessment, which indicates that risk characterizations should be based on the most sensitive indicator of toxicity. • EPA Risk Assessment Task Force's Staff Paper on Risk Assessment Principles and Practices, which indicates that cancer and non-cancer risks should be based on the most sensitive animal data. • EPA's A Review of the Reference Dose and Reference Concentration Processes, which indicates that the critical effect is defined as the first adverse effect that occurs to the most sensitive species as the dose rate of an agent increases. • EPA's policy on evaluating risks to children, which indicates that it is EPA policy to consider risks to infants and children. Documents by NAS (Science and Decisions: Advancing Risk Assessment; and Science and Judgment) also reiterate the need to protect the most sensitive subpopulations and to protect against the most sensitive endpoint. EPA's proposed risk determinations fail on both accounts. EPA asserts without evidence that "it is expected that addressing risks for these [immune system] effects would address other identified risks." EPA should be ashamed of itself.	
56, 108	**PUBLIC COMMENTS:** The TSCA requirement that EPA assess risks using the best available sciences necessitates that EPA base its risk determinations on congenital heart defects. • EPA scored studies of heart defects (Johnson et al., 2003 and Dawson et al., 1993) as "Medium" and has relied on Medium studies in its draft risk evaluations. • EPA indicated that congenital heart defects are the most sensitive	

	endpoint and did not identify contrary studies that were stronger or more reliable than the Johnson et al. (2003) study. • EPA's decision to ignore this endpoint in its final analysis based on the "best available science" is non-scientific and illogical; this decision was based on greater confidence in other endpoints (evidence that has no bearing on congenital heart defects). The best available science supports the use of the Johnson et al. (2003) study. EPA's approach of selecting the endpoint with the greatest confidence does not address other identified risks; it leaves risks from congenital heart defects insufficiently addressed, as indicated by the lower levels of exposure to TCE that cause those defects relative to exposure required to cause immune effects.	
56, 108	**PUBLIC COMMENTS:** EPA's decision to dismiss key immunotoxicity endpoints (decreased thymus weight and cellularity from Keil et al., 2009) and its decision to dismiss the Johnson et al. (2003) study as a representative chronic non-cancer study and using an alternative endpoint of autoimmunity from Keil et al. (2009) results in an approximately 9-fold underestimation of risk compared to what would have been calculated from the Johnson et al. (2003) study.	
69, 74	**PUBLIC COMMENTS:** The choice of immunosuppression (a 500-fold less sensitive endpoint) rather than fetal heart defects to assess risk fails to protect the most sensitive subpopulations, contradicts previous EPA assessments of TCE, existing EPA guidance, and expert advice of NAS, and promotes the false claim that risks for immune effects would address other identified risks.	
71, 73, 74	**PUBLIC COMMENTS:** The decision not to base risk determinations on fetal cardiac malformations is problematic because: • It is a departure from thoroughly peer-reviewed science, based on evidence of fetal cardiac malformations from the Johnson et al. (2003) and other epidemiological, *in vivo*, and *in vitro* studies. EPA	

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	and other scientific authorities (including the EPA SAB) have examined and affirmed the importance of fetal cardiac malformations. • It fails to protect sensitive populations because fetal cardiac malformations are directly relevant to the PESS of pregnant women, infants, and children. • It represents a deviation from EPA policies based on previous assessments of TCE and existing EPA guidance to use the most sensitive endpoint and protect the most sensitive group. EPA and NAS documents indicate that if EPA protects against the most sensitive endpoint, it will protect against other effects. A recommendation by SACC to support the decision to use immune endpoints rather than fetal cardiac endpoints for risk determinations on TCE is counter to the WOE and years of peer review, ignores TSCA's mandate to protect sensitive subpopulations, and disregards EPA policies on the selection of the most sensitive endpoints for modeling. The public health consequences of this choice will be substantial, allowing EPA to develop regulations 500-fold less protective for acute risks and 10-fold less protective of chronic risks.	
83	**PUBLIC COMMENTS:** Regulate to prevent TCE exposure now, refuting the Johnson (2003) study later, if possible. The two agencies that attempt to refute the findings of the Johnson study are associated with the chemical industry and could profit by being able to sell more TCE. Available data indicate that fetal cardiac defects occur at doses 500 times lower than the immune diseases that EPA is using for the maximum allowable exposure; therefore, stricter regulations must be maintained. The use of a 500 times higher maximum allowable exposure is putting corporate profit above human health. Regulation of EPA by the chemical industry (rather than the reverse) is not a new phenomenon, but it is strikingly more blatant.	
86	**PUBLIC COMMENTS:** We are gravely concerned with EPA's failure to identify fetal heart	

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	defects as the key risk of exposure to TCE, which will mean that when a woman's exposure to TCE during pregnancy is high enough to increase the risk of fetal heart defects, the chemical will not be regulated at a level to protect against that outcome. We demand that EPA address the major flaws it its draft risk evaluation to ensure that any future regulation of TCE protects the health of communities, including our most vulnerable, across the country.	
100	**PUBLIC COMMENTS:** In a departure from prior EPA risk assessments, EPA fails to base its calculations of TCE's risk on that most sensitive endpoint. As a result, any regulation of TCE under TSCA will not adequately protect against fetal cardiac malformations or neurodevelopmental impairment.	
106	**PUBLIC COMMENTS:** EPA's rationale for changing the representative acute non-cancer endpoint is unclear and inconsistent in the draft risk evaluation. EPA's choice of a representative acute non-cancer endpoint is less sensitive, less protective of vulnerable populations, and not consistent with best practices in scientific evaluation and use.	
106	**PUBLIC COMMENTS:** By pursuing the representative endpoint of immunosuppression, EPA would be allowing acute exposures significantly greater than the POD for fetal cardiac defects. While EPA still concluded that TCE presented an unreasonable risk for many COUs, the use of a more sensitive endpoint would have resulted in more protective unreasonable risk determinations for workers, ONUs, consumers, and bystanders. Choosing an immune endpoint would also fail to account for the sensitivity represented by developmental endpoints, as "…certain developmental effects may result from a single exposure during a critical window of development." It is a health-protective assumption that repeated exposure is not required for the manifestation of developmental toxicity. Choosing the immune endpoint in comparison to the fetal cardiac defects means discarding a more sensitive endpoint that has evidence of hazard to human health and which accounts for	

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	potentially exposure to susceptible subpopulations (fetuses, pregnant women, infants, and children). Considering the disparities between PODs for the two endpoints and the potential health ramifications due to this inadequately representative non cancer endpoint for TCE, EPA should use fetal cardiac defects as the basis of the non-cancer acute health effects and the subsequent risk assessment. EPA needs to give deference to the nature of this endpoint, and the sensitive nature as it impacts a vulnerable developmental period. This is particularly relevant as EPA's has a mandate under TSCA to ensure the protection of vulnerable populations such as these from unreasonable risks.	
108	**PUBLIC COMMENTS:** EPA justifies its selection of immunosuppression based on the highest quality evidence, the "best available science," independent verification, and weight of the scientific evidence. • EPA strayed from the requirements of Section 26 TSCA by basing selection on the quality of the Selgrade and Gilmour (2010) study. • There was an extensive consideration of the WOE supporting the congenital heart defects endpoint (and scrutiny of the Johnson et al., 2003 study), but the immunosuppression endpoint and other studies were not similarly scrutinized. • With respect to the independent verification requirement of TSCA, there is as much evidence for congenital heart defects as there is for immune effects. On p. 220, the draft risk evaluation concedes that there are no other data on respiratory immunosuppression and provides no supporting data for immunosuppression. For congenital heart defects, EPA notes that a HSIA-funded study showed a partial replication of results consistent with heart defects. These data and supporting epidemiological and mechanistic data make a strong case for congenital heart defects as a real, sensitive endpoint, protection against which is likely to be protective of other TCE-induced endpoints.	
108	**PUBLIC COMMENTS:** The use of these immune endpoints for POD derivation and subsequent	

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	risk determination would not protect against a constellation of more sensitive health effects that have been demonstrated in the literature to occur close to the range of the POD for congenital heart defects derived from the Johnson et al. (2003) study. Existing evidence and EPA precedent indicate that using the Johnson et al. (2003) study for POD derivation is well-justified and would protect against these numerous additional effects. • As noted in the IRIS 2011 Toxicological Review of TCE, the POD from the Johnson et al. (2003) study supported an RfD (of 0.0005 mg/kg-day, based on multiple effects) within 20% of candidate RfDs for other critical effects, including developmental immunotoxicity, decreased thymus weights, and kidney effects.	
108	**PUBLIC COMMENTS:** In the draft risk evaluation (p. 235), EPA presents six criteria for evaluation of candidate health domains, studies, and PODs (data quality evaluation score, species, exposure duration, dose range, cumulative uncertainty factor, and relevance to the endpoint of interest and human exposure scenarios). • EPA does not justify its endpoint/POD selection (especially given the difference in sensitivity between immunosuppression and congenital heart defects endpoints) because it addresses only some of these criteria (*i.e.,* data quality) for immunosuppression but does not provide a comparable evaluation for other health domains, studies, or PODs. EPA would be best served by considering both the WOE supporting the endpoint and its sensitivity. Immunosuppression and congenital heart defects endpoints were of adequate quality for dose-response modeling; subsequently, endpoint sensitivity should be expected to drive POD selection to best protect public health.	
108	**PUBLIC COMMENTS:** EDF strongly believes that the evidence for congenital heart defects is both compelling and amendable to dose-response modeling. EDF also believes that EPA must rely on this endpoint to ensure that it is in fact	

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	protecting the most vulnerable subpopulation from the risks of TCE exposure.	

7. Overall Content and Organization

Overall Content and Organization		
Charge Question 7.1: Please comment on the overall content, organization, and presentation of the TCE draft risk evaluation. Please provide suggestions for improving the clarity of the information presented. **Charge Question 7.2:** Please comment on the objectivity of the information used to support the risk characterization and the sensitivity of the agency's conclusions to analytic decisions made.		
#	**Summary of Comments for Specific Issues Related to Charge Question 6**	**EPA/OPPT Response**
Clarity and completeness of report		
SACC	**SACC COMMENTS:** Not all committee members agreed that the report structure is the easiest format to follow.	These organizational comments are appreciated and will be considered in a revised template for the next round of chemicals to be evaluated under TSCA section 6.
SACC	**SACC COMMENTS:** Recommendation: Implement the following revisions to improve clarity of the draft risk evaluation: • Cite original sources instead of referring to documents in the docket or to the EPA Web Application Access database where the public may not have easy access. • On Table 2-3 where estimates for the number of facilities for each OES are provided, the estimation of the number of facilities could be enhanced by adding a sense of uncertainty +/- X percent or X facilities. • The choice of a tornado graph in Figure 2-1 does not seem to be the best one to promote clarity. It is suggested that a set of pie charts or sectioned bar graph may better illustrate the point. • Section 2.2.5 mentions surface water concentration maps that are not provided. The color coding is provided but the maps themselves not provided nor is there a link or reference to their source. • Section 5.1.3 is simply not clear on the final environmental risk determination. From Section 4.1, one can deduce that no	With respect to citing original sources and using links in table to link to other tables, these organizational comments are appreciated and will be considered in a revised template for the next round of chemicals to be assessed under TSCA section 6. EPA does not have reasonably available data to conduct such an analysis for TCE. EPA's analysis uses TRI (U.S. EPA, 2017g) and DMR (U.S. EPA, 2016a) to estimate the highest local per site water releases of TCE. The tornado graph noted by the commenter did not communicate anything in addition to the text and therefore has been removed. Section 2.2.5 has been updated to include the

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	unreasonable risk to aquatic organisms in surface water was concluded. There are some risks with RQ >1 associated with specific facilities and species, but there is no summary of either in the final risk determination. It is recommended that the risk evaluation summarize the approach and determination for each COU. • Expand use of links in tables to other tables and include links to items in the docket.	surface water maps, which were previously only included in the environmental risk characterization sections.
SACC	**SACC COMMENTS:** Committee members commented that the SSD diagram (a scatterplot) is a good visualization tool to display the potential relative impact of chemical exposure on different species buts its utility depends on understanding the ecology of the aquatic environment.	EPA agrees with this comment and added further explanation around the SSD analysis in section 3 of the Risk Evaluation.
SACC	**SACC COMMENTS:** Recommendation: Provide more clarity on how cancer risks were estimated by showing computation details. A Committee member noted the development of cancer risk is difficult to ascertain. In this section (p. 250, lines 2463-2476), the draft risk evaluation states that the IUR is "adjusted by a factor of 4 to account for estimating risk from all three cancer types," yet later suggests that lifetime cancer risks are first calculated and then summed across all three types. Which is it?	From Section 3.2.5.3.3 of the Risk Evaluation, for the IUR "extra lifetime cancer risks were summed across the three cancer types and the ratio of the sum of the extra risks to the extra risk for kidney alone was derived." This ratio rounded to 4 from two different calculation methods. For the oral slope factor, "individual IUR estimates were first obtained for each site based on the ratios of extra risk relative to kidney. Those site-specific IUR estimates were then extrapolated to the equivalent OSFs using site-specific dose metrics, and those individual OSFs were summed to obtain a ratio of 5.0 relative to kidney cancer alone." Full details are available in Section 5.2.2 of the 2011 IRIS Assessment (U.S. EPA, 2011c).
SACC	**SACC COMMENTS:** The draft risk evaluation states that, in general, immunotoxic effects in animals and humans were associated with an enhanced immune	EPA has clarified that the thymus findings are not adverse and are not considered as a basis for

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	response rather than an immunosuppressive effect (draft risk evaluation, p. 212, lines 839-840). However, the first paragraph on animal data (draft risk evaluation, p. 213, lines 872-880) suggests that support for immunotoxicity is provided by decreased thymus weight and cellularity in mice, although the cellularity effect is not significant (Keil et al., 2009). The Committee recommended the risk evaluation not put indicators of immune-enhancement and immunosuppression in the same category and think more about MOA where these processes and indicators are different.	the POD from Keil et al., 2009.
106	**PUBLIC COMMENTS:** Not only is Chapter 3 (Hazards) in conflict with Chapter 5 (Risk Determination), it is also in conflict with itself *within Chapter 3* of the draft risk evaluation for TCE.	EPA respectfully disagrees with this comment. Section 5 uses language and hazard determinations that are consistent with conclusions from Section 3.
Insufficient time to review		
44	**PUBLIC COMMENTS:** Even before the COVID-19 crisis, the time frame EPA provided for getting meaningful expert review of this important document was already questionable. Now it is simply untenable. Proceeding with a virtual meeting is asking far too much of SACC members and their families and will clearly lead to a severely compromised peer review. We cannot let the current crisis result in a weakening of the quality and credibility of scientific input on other important public health issues. EPA needs to promptly postpone the SACC peer review of TCE and reschedule it at a time and in a manner that respects the critical role the SACC plays.	Thank you for expressing your concern. Due to the outbreak of the novel coronavirus, SARS-CoV-2, the cause of COVID-19, the agency implemented this change out of an abundance of caution and in response to travel restrictions imposed by some SACC members' employers and other members' concerns regarding travel, as communicated in the Federal Register on March 20, 2020 (85 FR 16096) (FRL-10006-79).
51	**PUBLIC COMMENTS:** The health effects information available for cardiac effects related to TCE exposure raises fundamental scientific questions that require careful deliberation and that can be informed by stakeholder input. We hope that you will take the necessary time to receive input from the ACC and others. EPA should resist pressure to expedite SACC's review of the draft.	Thank you for your comment. EPA will consider stakeholder inputs provided during the comment period.

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52	**PUBLIC COMMENTS:** Because of the limited time allowed for public comment, a critical review of the search strategy described in the 2017 document relative to that reported in the draft risk evaluation could not be conducted. Thus, at this time, comments are limited to examples (emphasizing that this is not a comprehensive list) of aspects that highlight the lack of transparency and reproducibility.	Thank you for your comment. EPA provides a 60-day public comment period on draft TSCA risk evaluations.
52	**PUBLIC COMMENTS:** Given the voluminous nature of the assessment, and the aggressive timeline provided for peer review, it is impossible to fully evaluate this aspect of the TCE draft risk evaluation (*i.e.,* scoring criteria not implemented as described in guidance) given that it would require a fully independent review of each study quality evaluation.	Thank you for your comment. EPA provides a 60-day public comment period on draft TSCA risk evaluations.
82, 86	**PUBLIC COMMENTS:** We request that EPA suspend the public comment period for the TCE draft risk evaluation while President Trump's national emergency declaration remains in effect and provide at least 60 days for comment once the national emergency is lifted. There is no capacity to focus on the draft TCE risk evaluation until the national emergency is over.	Thank you for your comment. EPA provided a 60-day public comment period on the draft TCE risk evaluation and due to the outbreak of the novel coronavirus, SARS-CoV-2, the cause of COVID-19, the agency implemented a virtual public meeting out of an abundance of caution and in response to travel restrictions imposed by some SACC members' employers and other members' concerns regarding travel, as communicated in the Federal Register on March 20, 2020 (85 FR 16096) (FRL-10006-79).
86, 87	**PUBLIC COMMENTS:** EPA's refusal to hold a public meeting or to extend the comment period is deeply concerning. We renew our request for a public meeting on TCE and request that it be scheduled at a time and in a manner and venue that accounts for disruptions caused by COVID-19 (fully accessible virtual meeting may be an option). The SACC meeting is not an appropriate venue for robust community participation.	Thank you for expressing your concern. Due to the outbreak of the novel coronavirus, SARS-CoV-2, the cause of COVID-19, the agency implemented this change out of an abundance of caution and in response to travel restrictions imposed by some SACC members' employers and other members' concerns

		regarding travel, as communicated in the Federal Register on March 20, 2020 (85 FR 16096) (FRL-10006-79).
47	**PUBLIC COMMENTS:** The 2-day lead time before a virtual prep meeting and the ~3 weeks granted for public comments to reach the peer review committee before it meets is inadequate. This reinforces the view that the current EPA approach values a calendar deadline for a decision over the integrity of the information going into the decision. Furthermore, the process appears to be a mechanism to discourage comments from the stakeholder community.	Thank you for your comment. EPA provided a 60-day public comment period on the draft TCE risk evaluation and due to the outbreak of the novel coronavirus, SARS-CoV-2, the cause of COVID-19, the agency implemented a virtual public meeting out of an abundance of caution and in response to travel restrictions imposed by some SACC members' employers and other members' concerns regarding travel, as communicated in the Federal Register on March 20, 2020 (85 FR 16096) (FRL-10006-79).
104	**PUBLIC COMMENTS:** We believe that the comment deadline provided by EPA for this chemical is too short under normal circumstances to expect substantial tribal comment for reasons expressed previously by us regarding other TSCA-related comment opportunities. At this time in history, the comment periods for TCE and other draft evaluations out under TSCA, which so impact tribes, clearly are inadequate.	Thank you for your comment. EPA provides a 60-day public comment period on draft TSCA risk evaluations
Concerns regarding virtual SAAC meeting		
57, 74, 108	**PUBLIC COMMENTS:** EPA's decision to hold the meeting as a virtual meeting during the Covid-19 public health crisis, poses a number of serious obstacles and challenges to ensuring that the peer review is conducted in a manner that complies with the Federal Advisory Committee Act.	Thank you for expressing your concern. Due to the outbreak of the novel coronavirus, SARS-CoV-2, the cause of COVID-19, the agency implemented this change out of an abundance of caution and in response to travel restrictions imposed by some SACC members' employers and other members' concerns regarding travel, as communicated in the Federal Register on March 20, 2020 (85 FR 16096)

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		(FRL-10006-79).
70, 74, 108	**PUBLIC COMMENTS:** Some panel members were not able to participate in portions of the meeting. Panel members with unique/particular expertise were not able to participate on certain days or in certain sessions over the course of the week. EPA should make this information on participation available in the docket. There is specific concern that absence of some members could result in skewing of the panel.	Thank you for your comment. The Final Report and Meeting Minutes of the TCE TSCA SACC virtual public meeting are available for your review.
71, 108	**PUBLIC COMMENTS:** The SACC peer review panel lacked anyone with specific expertise in heart development. This is a serious omission that taints the strength of the peer review of the draft.	Thank you for your comment. The Final Report and Meeting Minutes of the TCE TSCA SACC virtual public meeting are available for your review.
References/data not publicly available (includes confidential business information [CBI])		
52, 60	**PUBLIC COMMENTS:** EPA has not made critical information related to the identification and selection of information available in the TCE draft risk evaluation. There is no (publicly available) HERO project for TCE under OPPT, which is a significant limitation to the transparency related to the selection and tagging of data. The use of the HERO platform and library that is specific to the TSCA risk evaluation should be clarified and all records and libraries made publicly available.	EPA made the full studies available to peer reviewers and included a list of the studies and their results in the docket in accordance with TSCA section 26(j) and 40 CFR 702.51. Data quality evaluations for each study are available in the supplemental files.
108	**PUBLIC COMMENTS:** In developing this draft risk evaluation, a large fraction of the information that EPA relied upon constituted health and safety studies. All such information not subject to two narrow exceptions needs to be made public.	EPA made the full studies available to peer reviewers and included a list of the studies and their results in the docket in accordance with TSCA section 26(j) and 40 CFR 702.51. Data quality evaluations for each study are available in the appendix and supplemental files.
51	**PUBLIC COMMENTS:** HSIA's attempts to obtain the raw data that formed the basis of the Johnson et al. (2003) study report have been unsuccessful. Examination of the spreadsheet provided by EPA (Johnson, 2009; HERO ID 783484)	Dates for the range of experiments performed are provided in (Johnson et al., 2005). Details are not available on the dates for individual animal

	reveals an absence of certain critical information, including, most importantly, dates for any of the individual treatment/control animals.	measurements. EPA acknowledges this deficiency in Appendix F.1.2.
Primary references not reviewed – using data from other assessments (*e.g.*, IRIS, ATSDR)		
SACC	**SACC COMMENTS:** The Committee commented in general, the draft risk evaluation does a good job of explaining how the TSCA assessment differs in scope and focus from the IRIS assessment. Moreover, it is mentioned in multiple places that the hazard and risk assessments done previously are used as a starting point and then updated for the present assessment. However, a more informative summary could be provided, for example, that lists the critical endpoints for acute and chronic non-cancer and cancer effects, and the critical studies identified for each endpoint and/or those that were used to determine POD values.	These organizational comments are appreciated and will be considered in a revised template for the next round of chemicals to be evaluated under TSCA section 6.
33	**PUBLIC COMMENTS:** It is recommended that charge questions be added to address the following systematic review elements as applied in the TCE draft risk evaluation: • The appropriateness and transparency of partially relying on previous EPA assessments for selected aspects of the risk evaluation (*e.g.*, hazard characterization) but not others (*e.g.*, POD selection)	These comments with respect to additional charge questions are appreciated and will be considered in the next round of chemicals to be assessed under TSCA section 6.
52, 60	**PUBLIC COMMENTS:** There is a significant amount of ambiguity as to how studies identified in previous assessments were "leveraged." Such assessments were also described as a "starting point," which seems to be in contrast with that which is leveraged from previous assessment.	For human health hazard studies, the systematic review literature search only covered the period following publication of the IRIS assessment after 2010, because EPA leveraged the previously-peer reviewed analysis performed for that assessment which identified key and supporting studies. These studies were combined with relevant data published after the IRIS assessment and considered together in the Risk Evaluation.
Biased presentation of results		

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SACC	**SACC COMMENTS:** Recommendations: (1) Provide support for the statement on kidney cancer MOA or modify the statement to reflect the lack of consensus. (2) Provide more discussion in the body of the draft risk evaluation to support the statement in the Executive Summary on the kidney cancer MOA. The Executive Summary, p. 30, lines 1237-1240 states: "A linear non-threshold assumption was applied to the TCE cancer dose-response analysis because there is sufficient evidence that TCE-induced kidney cancer operates primarily through a mutagenic mode of action while it cannot be ruled out for the other two cancer types." One Committee member was uncertain that this is a correct statement, being unaware that there is consensus on the kidney cancer MOA. This may have arisen from the fact that the discussion in Section 3.2.4.2.2 – Kidney Cancer MOA only references the TCE 2011 IRIS assessment but provides no details in support of the statement above.	EPA has added some references acknowledging uncertainty in the genotoxic MOA for kidney cancer, however EPA believes it is the most likely mechanism. EPA has inserted the word "likely" in front of "operates." EPA also copied language into the Executive Summary from Section 3.2.4.2.2 which states that the linear assumption is also supported by "the positive associations observed via meta-analysis for all three cancers in epidemiological studies based on low-level, environmental exposure levels."
Concerns about TSCA systematic review approach/process		
SACC	**SACC COMMENTS:** Several Committee members commented that overall, it seems that EPA judges study quality, but it is difficult to understand how study relevance factors into any conclusion in choosing a particular study from which to develop a POD and resulting value to carry through the risk assessment.	EPA describes the factors considered when selecting studies and PODs to represent each endpoint in Section 3.2.5.3, of which "relevance to the endpoint of interest and human exposure scenarios" is included.
33, 47, 49, 99	**PUBLIC COMMENTS:** It is recommended that charge questions be added to address the following SR elements as applied in the TCE draft risk evaluation: • The soundness and reproducibility of the approach to identify and select studies for the underlying evidence base; specifically, the transparency, objectivity , and consistency of the approach implemented (*e.g.,* use of a bibliography to split studies into " on-topic" and "off-topic" categories). • The appropriateness of using the TSCA systematic review tool to evaluate individual study quality in one step of the assessment and a	These comments with respect to additional charge questions are appreciated and will be considered in the next round of chemicals to be evaluated under TSCA section 6.

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	completely different (and novel) tool to assess relevance and reliability in the WOE assessment. • The consistency in outreach to study authors to address questions in reporting. • The appropriateness of applying study quality criteria related to use of a positive control for some studies but not all, specifically the soundness of downgrading studies that did use a positive control, while not scoring this element for studies that lacked a positive control. • The appropriateness of deviating from the TSCA systematic review guidance on scoring to categorize *in vitro* studies that did not evaluate cytotoxicity and scored them as "NA" instead of "unacceptable." • The appropriateness, transparency, and consistency of subjective judgments to up- or down-grade study quality. • The soundness of the novel WOE approach utilized in the draft risk evaluation relative to standard systematic review approaches, such as GRADE, that have been previously recommended to EPA by the NAS. • The appropriateness of applying the novel WOE framework to assess hazard potential of only one of the several endpoints assessed in the draft risk evaluation. • The completeness of data integration; specifically, the adequacy of the evaluation of consistency, coherence, and biological plausibility as part of the data integration step for each endpoint (as is described in Figure 3-3 of the TCE draft risk evaluation).	
47, 49, 99	**PUBLIC COMMENTS:** Feedback on the draft systematic review guidance is needed now; however, the NAS review of this guidance is not yet available. As the NAS belatedly reviews the guidance, EPA should cease using it in final risk evaluations but instead apply one of the recognized systematic review methodologies.	EPA's systematic review is currently based on *Application of Systematic Review in TSCA Risk Evaluations*. Revisions to systematic review are under development (*Systematic Review Protocol Supporting the TSCA Risk Evaluations*); EPA anticipates feedback from the NASEM TSCA
49, 99	**PUBLIC COMMENTS:**	

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	The TSCA method departs radically from accepted scientific principles for systematic review adopted by the Institute of Medicine (IOM), NTP and IRIS and endorsed by the NAS and other peer review bodies. The SACC has "noted problems with both the systematic review design and consistent implementation of its protocols." At a minimum, EPA's final risk evaluations must respond fully to the SACC's comments.	Committee on its systematic review process, including the epidemiological data quality criteria. EPA/OPPT's quality evaluation method was developed following identification and review of various published qualitative and quantitative scoring systems to inform our own fit-for-purpose tool. The development process involved reviewing various evaluation tools/frameworks (*e.g.,* OHAT Risk of Bias tool, CRED, etc.; see Appendix A of the Application of Systematic Review in TSCA Risk Evaluations document and references therein), as well as soliciting input from scientists based on their expert knowledge about evaluating various data/information sources specifically for risk assessment purposes. The epidemiologic criteria were later revised to more stringently distinguish between High, Medium and Low studies. After additional piloting of the criteria, EPA found that the initial iteration of the epi data quality criteria (as published in the Application of Systematic Review in TSCA Risk Evaluations) was inadvertently skewing quality scores toward the tail ends of the scoring spectrum (High and Unacceptable). In order to have the criteria represent a more accurate depiction of the quality levels in the epi literature, the criteria were revised using two methods.
56, 73, 74, 99	**PUBLIC COMMENTS:** Ratings are based on a profoundly, and fundamentally, flawed systematic review method. Those flaws include the lack of any empirical support for the scoring system devised, use of numerical scores to characterize study quality as a general matter, and lack of a defined procedure for data integration, among others. The use of numerical study scoring defies consistent recommendations in the field of systematic review including those made in the 2014 Academies review of the IRIS program.	
106	**PUBLIC COMMENTS:** EPA's scoring method wrongly downgrades or excludes a study based on a reporting deficiency, conflating how well a study is reported with how well the underlying research was conducted. Although EPA has posted its "Updates to the Data Quality Criteria for Epidemiological Studies," EPA's TSCA method still uses reporting measures in its scoring of the quality of human studies; this includes incorporating reporting guidelines into the rationales for scoring studies "low quality" (Metrics 1 and 15) or "unacceptable for use" (Metrics 3, 4, 6, 7). Using STROBE reporting guidelines to score individual studies is contrary to the recommendations given by the authors of the STROBE guidelines, who specifically note that the guidelines are not a measure of the quality of the underlying research. • The inclusion of numerous reporting items irrelevant to bias in a quality scoring rule (*e.g.,* an indicator of whether power calculations were reported), will disproportionately reduce some of the resulting scores and erroneously undervalue the study quality.	
106,	**PUBLIC COMMENTS:**	

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49, 99	The use of a scoring system that excludes a study based on only one criterion/metric directly contradicts widely accepted systematic review methodological approaches (*e.g.,* NTP OHAT, UCSF Navigation Guide), and it will almost certainly result in flawed conclusions and threaten the protection of the public's health. This approach is also inconsistent with TSCA mandates to use the "best available science" and "reasonably available information," while discussing its "strengths and limitations."	The first method was to make the unacceptable metrics less stringent. This was accomplished by either rewording the metrics to allow for more professional judgement in the interpretation of the unacceptable criterion, or in some cases, completely removing the unacceptable bin from metrics that EPA determined were not influential enough to completely disqualify a study from consideration (mostly metrics in the Analysis and Biomonitoring domain). EPA found that these criteria changes greatly reduced the type one error in the Unacceptable scoring. No acceptable studies were inaccurately classified as Unacceptable. The second method was to reduce the number of studies that received an overall High rating. The majority of overall scores in EPA's initial evaluations during piloting tended to be High. Therefore, EPA strived to revise the criteria to provide more degradation in the scoring to more accurately and objectively distinguish studies of the highest quality from medium and low quality studies. To do this, EPA removed the High criterion from some metrics, particularly in dichotomous metrics (High/Low or High/Unacceptable) that were primarily being binned as High by reviewers across the majority of the studies. These dichotomous metrics were contributing to the overall quality scores being skewed towards High. To address this, EPA shifted some of the dichotomous metrics such that the highest metric score possible (for all
106, 49, 99	**PUBLIC COMMENTS:** We strongly urge EPA to remove the option to rate a study "Unacceptable" from every metric as the underlying assumptions of EPA's "serious flaws" metrics are not evidence-based, specifically: • EPA's list of "serious flaws" are not all equal indicators of study quality. • EPA's list of "serious flaws" are not all related to real flaws in the underlying research (*i.e.,* reporting guidelines are wrongly equated with serious flaws in study quality. Analysis is equated with a "serious flaw" in study quality, but statistical power is not a valid measure of study quality and should not be used to disqualify studies from consideration. EPA's Metric 13 statistical power/sensitivity confuses bias with imprecision. Individual studies that are "underpowered" (*e.g.,* because in the real world, the exposed population may not be large enough for statistical purposes even if they are health-impacted) can still be potentially valuable to evidence-based decision-making. Underpowered studies that find a health effect to be present may be indicative of a larger effect size than anticipated; omitting or downgrading such studies due to being underpowered would severely bias the conclusions of the review.	
56	**PUBLIC COMMENTS:** OPPT provides neither an explanation nor empirical support for its revisions to the systematic review data quality criteria for epidemiological studies, which makes it more difficult for epidemiological studies to be scored overall as high quality. This	

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	underscores that the study quality evaluation strategy that OPPT developed is not evidence-based.	studies) is a Medium. The change led to the dichotomous metrics having less significant impact to the numerical scoring and the overall quality rating for each study. With the aforementioned changes to the criteria, EPA observed fewer studies with Unacceptable ratings and more studies shifting from High to Medium, with only the highest quality studies receiving a High overall rating. Out of the ~200 relevant epidemiologic studies and cohorts evaluated for data quality for the first 10 TSCA chemicals, the majority (~80%) still scored as High or Medium. The remaining ~20% of studies scored Low or Unacceptable. EPA is confident that no studies of acceptable quality were inappropriately assigned as Unacceptable. EPA is also confident that the revised criteria bins the quality levels of these epi studies more appropriately than the previous iteration. Additional refinements to the epidemiologic data evaluation criteria are likely to occur as EPA's validation and process improvement efforts continue.
56, 108	**PUBLIC COMMENTS:** At least six metrics in EPA OPPT's updated epidemiological criteria can no longer receive a score of High, including Metric 5 (Exposure Levels) and Metric 15 (Statistical Models). Since these individual metrics can at best be rated as Medium (a change from the earlier epidemiological criteria), epidemiological studies are thus less likely to be considered high quality overall, and as a result, may be given more limited consideration than other types of evidence (animal and *in vitro* studies), where it is remains possible to score High across every data quality metric.	
56, 108	**PUBLIC COMMENTS:** EPA should consider other study evaluation tools that are more appropriate for the consideration of the quality of observational epidemiologic studies. Examples include the Conducting Systematic Reviews and Meta-Analyses of Observational Studies of Etiology (COSMOS-E) tool and the Navigation Guide.	
Inappropriate application of systematic review for TCE		
52	**PUBLIC COMMENTS:** The TCE draft risk evaluation was not compliant with systematic review. Only two of the key elements were completed by EPA in their systematic review (a clearly stated set of objectives and interpretation of results/presentation of a summary of findings); other key elements were either completely absent or were inconsistent/incomplete.	Because EPA was developing the systematic review process while simultaneously implementing the process for ten chemicals, there were some challenges with maintaining consistency. However, EPA did implement several steps to ensure consistency and reduce bias. EPA used calibration steps among multiple

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		screeners during a pilot phase for both the data screening and data evaluation processes. Furthermore, instructions were prepared for various aspects of the systematic review (*e.g.,* data screening, data evaluation, and data extraction) to guide the reviewers and provide consistency across reviews. Finally, most studies received two data quality evaluations with reviewers working together to resolve conflicts, sometimes with a single arbiter across similar types of studies. EPA has implemented additional calibration steps and internal guidance documents for the next 20 chemicals going through the systematic review process now. Any single set of data quality criteria, even for a given category of studies (*e.g.,* animal toxicity studies), cannot necessarily address all aspects of quality relevant for an individual study in the category. Thus, EPA allowed reviewers the ability to adjust the final score based on professional judgment. This approach has been used in other established tools, including the ToxRTool (Toxicological data Reliability Assessment Tool) developed by the European Commission (https://eurl-ecvam.jrc.ec.europa.eu/about-ecvam/archive-publications/toxrtool). EPA implemented a literature search process for the first ten chemicals that included a comprehensive set of key words to capture as much of the literature for a given discipline as

		possible. However, even with a comprehensive literature search, some important studies may be missed. For instance, an abstract may not identify the chemical of interest by name (*e.g.,* if a genotoxicity test was conducted on many chemicals) and thus might be screened out from further consideration. In addition, some targeted searching for topics not anticipated at the beginning of the risk evaluation process (*e.g.,* generic inputs needed for an exposure model) might be needed. Therefore, such backwards searching (or snowballing) and targeted searching remain important aspects of the systematic review process. EPA will publish a protocol document for the next TSCA risk evaluations. Furthermore, EPA anticipates feedback from the NASEM TSCA Committee on its systematic review process and will carefully review their recommendations for the next 20 chemicals.
52, 56, 108, 49, 99	**PUBLIC COMMENTS:** The lack of a protocol resulted in numerous arbitrary and inconsistent decisions, lack of structured and systematic syntheses, and lack of transparency throughout the risk evaluation. No protocol was developed for TCE, rather, planning documents were limited to a scoping document, a strategy for literature search, and a bibliography file. OPPT has not provided a pre-established methodology for its approach to evidence integration. OPPT needs to develop full protocols for each of its risk evaluation and should consult with the IRIS program on how best to do so in consideration of requirements under TSCA.	Because EPA was developing the systematic review process while simultaneously implementing the process for ten chemicals, there were some challenges with maintaining consistency. However, EPA did implement several steps to ensure consistency and reduce bias. EPA used calibration steps among multiple screeners during a pilot phase for both the data screening and data evaluation processes. Furthermore, instructions were prepared for various aspects of the systematic review (*e.g.,*

		data screening, data evaluation, and data extraction) to guide the reviewers and provide consistency across reviews. Finally, most studies received two data quality evaluations with reviewers working together to resolve conflicts, sometimes with a single arbiter across similar types of studies. EPA has implemented additional calibration steps and internal guidance documents for the next 20 chemicals going through the systematic review process now. Any single set of data quality criteria, even for a given category of studies (*e.g.,* animal toxicity studies), cannot necessarily address all aspects of quality relevant for an individual study in the category. Thus, EPA allowed reviewers the ability to adjust the final score based on professional judgment. This approach has been used in other established tools, including the ToxRTool (Toxicological data Reliability Assessment Tool) developed by the European Commission (https://eurl-ecvam.jrc.ec.europa.eu/about-ecvam/archive-publications/toxrtool). EPA implemented a literature search process for the first ten chemicals that included a comprehensive set of key words to capture as much of the literature for a given discipline as possible. However, even with a comprehensive literature search, some important studies may be missed. For instance, an abstract may not identify the chemical of interest by name (*e.g.,* if a

		genotoxicity test was conducted on many chemicals) and thus might be screened out from further consideration. In addition, some targeted searching for topics not anticipated at the beginning of the risk evaluation process (*e.g.,* generic inputs needed for an exposure model) might be needed. Therefore, such backwards searching (or snowballing) and targeted searching remain important aspects of the systematic review process. EPA will publish a protocol document for the next TSCA risk evaluations. Furthermore, EPA anticipates feedback from the NASEM TSCA Committee on its systematic review process and will carefully review their recommendations for the next 20 chemicals.
52	**PUBLIC COMMENTS:** There are many aspects of EPA's systematic review approach that are not reproducible – a reflection of the lack of compliance with systematic review methodologies and extensive subjective and inconsistent actions. These include the lack of transparency and systematic method for identifying evidence, lack of consistency in applying the data quality tool, lack of adherence to the criteria in applying the data quality tool, subjective decisions to up- and down-grade studies after applying the study quality tool, and developing and implementing a WOE approach during the conduct of the TCE risk evaluation.	Because EPA was developing the systematic review process while simultaneously implementing the process for ten chemicals, there were some challenges with maintaining consistency. However, EPA did implement several steps to ensure consistency and reduce bias. EPA used calibration steps among multiple screeners during a pilot phase for both the data screening and data evaluation processes. Furthermore, instructions were prepared for various aspects of the systematic review (*e.g.,* data screening, data evaluation, and data extraction) to guide the reviewers and provide consistency across reviews. Finally, most studies received two data quality evaluations with

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		reviewers working together to resolve conflicts, sometimes with a single arbiter across similar types of studies. EPA has implemented additional calibration steps and internal guidance documents for the next 20 chemicals going through the systematic review process now. Any single set of data quality criteria, even for a given category of studies (*e.g.,* animal toxicity studies), cannot necessarily address all aspects of quality relevant for an individual study in the category. Thus, EPA allowed reviewers the ability to adjust the final score based on professional judgment. This approach has been used in other established tools, including the ToxRTool (Toxicological data Reliability Assessment Tool) developed by the European Commission (https://eurl-ecvam.jrc.ec.europa.eu/about-ecvam/archive-publications/toxrtool). EPA implemented a literature search process for the first ten chemicals that included a comprehensive set of key words to capture as much of the literature for a given discipline as possible. However, even with a comprehensive literature search, some important studies may be missed. For instance, an abstract may not identify the chemical of interest by name (*e.g.,* if a genotoxicity test was conducted on many chemicals) and thus might be screened out from further consideration. In addition, some targeted searching for topics not anticipated at the

		beginning of the risk evaluation process (*e.g.,* generic inputs needed for an exposure model) might be needed. Therefore, such backwards searching (or snowballing) and targeted searching remain important aspects of the systematic review process. EPA will publish a protocol document for the next TSCA risk evaluations. Furthermore, EPA anticipates feedback from the NASEM TSCA Committee on its systematic review process and will carefully review their recommendations for the next 20 chemicals.
52, 60, 106	**PUBLIC COMMENTS:** The approach for identification of evidence is not systematic, transparent, or readily reproducible. For example: • There is a large time lag between searches described in the strategy and the conduct of the actual risk evaluation. • The generic flow charts in Figures 1-5 through 1-9 do not provide transparent documentation of how data were identified, nor do they align with the multitude of approaches described in the 2017 literature search strategy document. Documentation should be made publicly available for all records, by tag, in the figures. • Appendix B is missing almost 1000 'on-topic' study reports from the supplemental bibliography from the TCE scoping document, and there are an additional 35 studies which go missing between the 215 study reports in the cited supplemental bibliographies for the draft risk evaluation, and the 180 studies referenced in Figure 1-9. Such inconsistencies are deeply concerning and threaten the validity of the draft risk evaluations. • In Figure 1-8, EPA includes the appropriate additional step of reporting the number of studies screened at the 'Title/Abstract' stage and the number at the 'Full Text Screening' stage while Figure 1-9	Because EPA was developing the systematic review process while simultaneously implementing the process for ten chemicals, there were some challenges with maintaining consistency. However, EPA did implement several steps to ensure consistency and reduce bias. EPA used calibration steps among multiple screeners during a pilot phase for both the data screening and data evaluation processes. Furthermore, instructions were prepared for various aspects of the systematic review (*e.g.,* data screening, data evaluation, and data extraction) to guide the reviewers and provide consistency across reviews. Finally, most studies received two data quality evaluations with reviewers working together to resolve conflicts, sometimes with a single arbiter across similar types of studies. EPA has implemented additional calibration steps and internal guidance documents

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	does not. • The draft risk evaluation does not describe how multiple platforms (DRAGON, DistillerSR, and HERO) were utilized to facilitate various aspects of the review. The 2017 document indicates that information from DRAGON was being migrated to DistillerSR, but it is not clear which platform was used for steps outside of the initial title and abstract screening for "on topic" and "off topic" selections. All of these platforms provide audit trails and produce output that could transparently document the identification and selection process. Such documentation should be made publicly available. • The articles identified by backwards searching should be clearly identified, and a narrative on the types and number of studies that were not identified in the initial search should be discussed. The 2017 document describes a process to evaluate the performance of the search strategies, though the results of such are not described in the draft risk evaluation. • The decision to skip data screening is unclear and should be clarified as to which data were not subject to screening as such an approach is not consistent with systematic review.	for the next 20 chemicals going through the systematic review process now. Any single set of data quality criteria, even for a given category of studies (*e.g.,* animal toxicity studies), cannot necessarily address all aspects of quality relevant for an individual study in the category. Thus, EPA allowed reviewers the ability to adjust the final score based on professional judgment. This approach has been used in other established tools, including the ToxRTool (Toxicological data Reliability Assessment Tool) developed by the European Commission (https://eurl-ecvam.jrc.ec.europa.eu/about-ecvam/archive-publications/toxrtool). EPA implemented a literature search process for the first ten chemicals that included a comprehensive set of key words to capture as much of the literature for a given discipline as possible. However, even with a comprehensive literature search, some important studies may be missed. For instance, an abstract may not identify the chemical of interest by name (*e.g.,* if a genotoxicity test was conducted on many chemicals) and thus might be screened out from further consideration. In addition, some targeted searching for topics not anticipated at the beginning of the risk evaluation process (*e.g.,* generic inputs needed for an exposure model) might be needed. Therefore, such backwards searching (or snowballing) and targeted searching

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		remain important aspects of the systematic review process. EPA will publish a protocol document for the next TSCA risk evaluations. Furthermore, EPA anticipates feedback from the NASEM TSCA Committee on its systematic review process and will carefully review their recommendations for the next 20 chemicals.
45, 67	**PUBLIC COMMENTS:** Based on a simple PubMed Search, it was estimated that there was ~2,200 published findings of toxicity on TCE; however, EPA finds only 419 ecotox and 170 human hazard. It was also suggested that the search query was too general, and that EPA should start again at the literature review stage or it will not be performing systematic review. Six studies were listed that were considered relevant, but were not included by EPA including a study on congenital heart effect (Harris et al., 2018). EPA should verify that none of the excluded studies from previous risk assessments were key studies.	Thank you for your comment. However, as shown in Figures 1-10 and 1-11, EPA identified 8,500+ and 6,000+ literature results for Environmental and Human Health Hazard, respectively. The majority of these studies were identified as off-topic and not relevant to the TCE Risk Evaluation based on title/abstract screening. The literature search ended in early 2017, so studies published after this date would not have been identified. (Harris et al., 2018) was included in the Risk Evaluation, however and is incorporated into the WOE analysis for cardiac malformations.
52	**PUBLIC COMMENTS:** Many studies that were relevant to the Populations, Exposures, Comparators, and Outcomes (PECO) statement and initially categorized as "on topic" were not considered in the TCE draft risk evaluation. The documentation is insufficient to understand why clearly relevant studies that were initially included were, at some later point, disregarded in the TCE draft risk evaluation (six studies were listed). • Cosby, NC; Dukelow, WR. (1992). Toxicology of maternally ingested trichloroethylene (TCE) on embryonal and fetal development in mice and of TCE metabolites on in vitro	EPA did consider the majority of these studies in the Risk Evaluation in the context of the cardiac defects WOE. EPA has added a clarification to Appendix F.3.1 that the following studies were screened out as off-topic for the cardiac defects WOE specifically because the study reports did not indicate direct assessment of cardiac defects, cardiovascular effects, or any related outcomes: (Beliles et al., 1980; Bross et al., 1983; Cosby

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	fertilization. Fundam Appl Toxicol. 19: 268-274. • Narotsky, MG; Kavlock, RJ. (1995). A multidisciplinary approach to toxicological screening: II. Developmental toxicity. J Toxicol Environ Health. 45: 145-171. http://dx.doi.org/10.1080/15287399509531987. • Caldwell, PT; Manziello, A; Howard, J; Palbykin, B; Runyan, RB; Selmin, O. (2010). Gene expression profiling in the fetal cardiac tissue after folate and low-dose trichloroethylene exposure. Birth Defects Res A Clin Mol Teratol. 88: 111-127. http://dx doi org/10 1002/bdra 20631. • Bross, G; Difranceisco, D; Desmond, ME. (1983). The effects of low dosages of trichloroethylene on chick development. Toxicology. 28: 283-294. http://dx doi org/10 1016/0300-483X(83)90002-1. • Elovaara, E; Hemminki, K; Vainio, H. (1979). Effects of methylene chloride, trichloroethane, trichloroethylene, tetrachloroethylene and toluene on the development of chick embryos. Toxicology. 12: 111-119. http://dx.doi.org/10.1016/0300-483X(79)90037-4. • Tola, S; Vilhunen, R; Jarvinen, E; Korkala, ML. (1980). A cohort study on workers exposed to trichloroethylene. J Occup Environ Med. 22: 737-740.	and Dukelow, 1992; Dorfmueller et al., 1979; Elovaara et al., 1979; Narotsky and Kavlock, 1995; Narotsky et al., 1995). The referenced Caldwell study is a follow-up to (Caldwell et al., 2008), which was included in the WOE analysis. This study examines gene expression changes following TCE exposure but does not provide any relevant novel information that would influence the WOE beyond what was already discussed from (Caldwell et al., 2008) and (Collier et al., 2003). The (Tola et al., 1980) study was not included in (Makris et al., 2016) or the 2014 TCE Work Plan Chemical Risk Assessment (U.S. EPA, 2014b), which were the sources for older studies (*i.e.,* would not have been captured in the literature search which only searched 2010-2017 studies) relevant to cardiac toxicity (as described in Appendix F3.1). It was also not identified as a key study from the 2011 IRIS Assessment (U.S. EPA, 2011e) because it did not contain dose-response information. Therefore, this study was not included in the risk evaluation for cardiac defects or other effects.
56	**PUBLIC COMMENTS:** EPA's use of studies here that are otherwise excluded through the PECO statement raises concern that EPA has introduced bias and inconsistency in the risk evaluation process. EPA should develop general guidance for when these allowances may be considered, and clearly identify, with supporting justification, those specific instances where studies excluded during systematic review or other processes can be referenced and relied on in developing the risk evaluation.	Because EPA was developing the systematic review process while simultaneously implementing the process for ten chemicals, there were some challenges with maintaining consistency. However, EPA did implement several steps to ensure consistency and reduce bias. EPA used calibration steps among multiple screeners during a pilot phase for both the data screening and data evaluation processes.

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		Furthermore, instructions were prepared for various aspects of the systematic review (*e.g.,* data screening, data evaluation, and data extraction) to guide the reviewers and provide consistency across reviews. Finally, most studies received two data quality evaluations with reviewers working together to resolve conflicts, sometimes with a single arbiter across similar types of studies. EPA has implemented additional calibration steps and internal guidance documents for the next 20 chemicals going through the systematic review process now. Any single set of data quality criteria, even for a given category of studies (*e.g.,* animal toxicity studies), cannot necessarily address all aspects of quality relevant for an individual study in the category. Thus, EPA allowed reviewers the ability to adjust the final score based on professional judgment. This approach has been used in other established tools, including the ToxRTool (Toxicological data Reliability Assessment Tool) developed by the European Commission (https://eurl-ecvam.jrc.ec.europa.eu/about-ecvam/archive-publications/toxrtool).
52, 60	**PUBLIC COMMENTS:** Data quality evaluations were not conducted in a systematic or reproducible manner – aspects of which will not be apparent to the SACC members without conducting an independent review of each study quality evaluation and, as such, it will be practically impossible for the SACC to critically evaluate the consistency across studies and evidence streams.	Because EPA was developing the systematic review process while simultaneously implementing the process for ten chemicals, there were some challenges with maintaining consistency. However, EPA did implement several steps to ensure consistency and reduce

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	• The scoring criteria were not implemented as described in the Draft EPA Systematic Review guidance; thus, entries are either inaccurate or intentionally scored differently than that described in the draft guidance without explanation to such (*e.g.,* Metric 9 for HERO ID 65163; Metric 6 for HERO ID 62111). • Data quality scores were applied inconsistently across studies (specific examples and HERO IDs were provided). Examples included Metric 2 (test substance source; 2 studies that failed to report source, one was rated medium, one was rated low), Metric 5 (positive controls; should not be not rated for teratogenicity studies) and Metric 19 (blinding; should not be scored for initial histopathology). Inconsistency in metric scoring is a re-occurring feature across the score sheets, suggesting insufficient reviewer oversight and quality control measures in the scoring process. Scoring inconsistencies introduce additional uncertainty into what is already a highly subjective evaluation process, further calling into question EPA's attempt at integrating the evidence streams related to in utero exposures to TCE and development of fetal cardiac defects into a coherent conclusion. • Data quality scores were subjectively altered based on judgments for aspects not addressed by the data quality criteria (*i.e.,* were altered for reasons, such as relevance, which should be addressed in a different step of the systematic review). There were many instances in the data quality evaluation that TSCA relied on quality elements related to relevance and applicability (which relate to construct and external validity) rather than assessing the quality based on internal validity as described in the guidance. That is, many subjective judgments were made based on data quality criteria that were not actually part of the data quality tool. These subjective judgments were not consistent within and across the evidence base, nor are they reproducible (two examples were provided in a table). • Data quality scores were subjectively altered based on the results of the study rather than the methodological and reporting quality,	bias. EPA used calibration steps among multiple screeners during a pilot phase for both the data screening and data evaluation processes. Furthermore, instructions were prepared for various aspects of the systematic review (*e.g.,* data screening, data evaluation, and data extraction) to guide the reviewers and provide consistency across reviews. Finally, most studies received two data quality evaluations with reviewers working together to resolve conflicts, sometimes with a single arbiter across similar types of studies. EPA has implemented additional calibration steps and internal guidance documents for the next 20 chemicals going through the systematic review process now. Any single set of data quality criteria, even for a given category of studies (*e.g.,* animal toxicity studies), cannot necessarily address all aspects of quality relevant for an individual study in the category. Thus, EPA allowed reviewers the ability to adjust the final score based on professional judgment. This approach has been used in other established tools, including the ToxRTool (Toxicological data Reliability Assessment Tool) developed by the European Commission (https://eurl-ecvam.jrc.ec.europa.eu/about-ecvam/archive-publications/toxrtool). EPA implemented a literature search process for the first ten chemicals that included a comprehensive set of key words to capture as

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	which is regarded as a significant bias in evidence-based practice. The direction of result should not impact the objective assessment of methodological rigor and reporting quality (three examples were provided in a table). • Inconsistencies speak to insufficient reviewer oversight and quality control measures in the scoring process, including failure to get all reviewers on "the same page" with respect to interpreting and applying the metric scoring criteria. • Data quality scores demonstrate bias in reviewer evaluation (two examples were provided in a table).	much of the literature for a given discipline as possible. However, even with a comprehensive literature search, some important studies may be missed. For instance, an abstract may not identify the chemical of interest by name (*e.g.,* if a genotoxicity test was conducted on many chemicals) and thus might be screened out from further consideration. In addition, some targeted searching for topics not anticipated at the beginning of the risk evaluation process (*e.g.,* generic inputs needed for an exposure model) might be needed. Therefore, such backwards searching (or snowballing) and targeted searching remain important aspects of the systematic review process. EPA will publish a protocol document for the next TSCA risk evaluations. Furthermore, EPA anticipates feedback from the NASEM TSCA Committee on its systematic review process and will carefully review their recommendations for the next 20 chemicals.
56	**PUBLIC COMMENTS:** EPA's selective inclusion of studies otherwise excluded as part of its systematic review process raises concern around inconsistency and bias. EPA fails to identify which "unacceptable" studies were referenced for hazard identification and weight-of-the-scientific-evidence assessment, for which endpoints, and on what basis. Absent any explanation, let alone guidance, for when and how "unacceptable" studies may be considered during risk evaluation, EPA's ad hoc use of unacceptable studies introduces significant risk for arbitrary, biased, and inconsistent treatment of scientific evidence.	Because EPA was developing the systematic review process while simultaneously implementing the process for ten chemicals, there were some challenges with maintaining consistency. However, EPA did implement several steps to ensure consistency and reduce bias. EPA used calibration steps among multiple screeners during a pilot phase for both the data screening and data evaluation processes. Furthermore, instructions were prepared for

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		various aspects of the systematic review (*e.g.,* data screening, data evaluation, and data extraction) to guide the reviewers and provide consistency across reviews. Finally, most studies received two data quality evaluations with reviewers working together to resolve conflicts, sometimes with a single arbiter across similar types of studies. EPA has implemented additional calibration steps and internal guidance documents for the next 20 chemicals going through the systematic review process now. Any single set of data quality criteria, even for a given category of studies (*e.g.,* animal toxicity studies), cannot necessarily address all aspects of quality relevant for an individual study in the category. Thus, EPA allowed reviewers the ability to adjust the final score based on professional judgment. This approach has been used in other established tools, including the ToxRTool (Toxicological data Reliability Assessment Tool) developed by the European Commission (https://eurl-ecvam.jrc.ec.europa.eu/about-ecvam/archive-publications/toxrtool). EPA implemented a literature search process for the first ten chemicals that included a comprehensive set of key words to capture as much of the literature for a given discipline as possible. However, even with a comprehensive literature search, some important studies may be missed. For instance, an abstract may not identify

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		the chemical of interest by name (*e.g.,* if a genotoxicity test was conducted on many chemicals) and thus might be screened out from further consideration. In addition, some targeted searching for topics not anticipated at the beginning of the risk evaluation process (*e.g.,* generic inputs needed for an exposure model) might be needed. Therefore, such backwards searching (or snowballing) and targeted searching remain important aspects of the systematic review process. EPA will publish a protocol document for the next TSCA risk evaluations. Furthermore, EPA anticipates feedback from the NASEM TSCA Committee on its systematic review process and will carefully review their recommendations for the next 20 chemicals.
56	**PUBLIC COMMENTS:** OPPT's approach taken to evidence integration in the TCE draft risk evaluation does not align with best practices as reflected and shared by leading systematic review methods for chemical assessment (*e.g.,* OHAT, NavGuide, IRIS).	EPA's systematic review is currently based on *Application of Systematic Review in TSCA Risk Evaluations*. Revisions to systematic review are under development (*Systematic Review Protocol Supporting the TSCA Risk Evaluations*); EPA anticipates feedback from the NASEM TSCA Committee on its systematic review process, including the epidemiological data quality criteria, and will carefully review and implement relevant recommendations.
Conduct additional sensitivity analyses		
SACC	**SACC COMMENTS:** The Committee strongly supports the use of a sensitivity assessment of the consumer exposure model.	The assumptions and uncertainties associated with our consumer exposure evaluation is fully

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		described in Section 2.3.2.6. A description of the sensitivity analysis on the overall CEM model is described in Appendix D.3. Consumer exposures were evaluated across a range of user intensities by varying weight fraction of a product and the time and amount of a product used. These user intensities were expected to cover a range of possible consumer exposures.
106	**PUBLIC COMMENTS:** There is no empirical evidence demonstrating how each risk-of-bias domain should be weighted and the exclusion of studies based on an arbitrary rating of the evidence is not supported. If studies are to be excluded from a body of evidence, it is more appropriate to evaluate their influence on the overall effect estimates quantitatively using meta-analysis. Strategies including conducting sensitivity analyses which calculate overall effect estimates among high quality studies only or stratifying results based on overall study quality. Researchers may also choose to present all studies and qualitatively discuss the risk of bias using structured approaches, similar to OHAT and GRADE.	Because EPA was developing the systematic review process while simultaneously implementing the process for ten chemicals, there were some challenges with maintaining consistency. However, EPA did implement several steps to ensure consistency and reduce bias. EPA used calibration steps among multiple screeners during a pilot phase for both the data screening and data evaluation processes. Furthermore, instructions were prepared for various aspects of the systematic review (*e.g.,* data screening, data evaluation, and data extraction) to guide the reviewers and provide consistency across reviews. Finally, most studies received two data quality evaluations with reviewers working together to resolve conflicts, sometimes with a single arbiter across similar types of studies. EPA has implemented additional calibration steps and internal guidance documents for the next 20 chemicals going through the systematic review process now. Any single set of data quality criteria, even for a given category of studies (*e.g.,* animal toxicity

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		studies), cannot necessarily address all aspects of quality relevant for an individual study in the category. Thus, EPA allowed reviewers the ability to adjust the final score based on professional judgment. This approach has been used in other established tools, including the ToxRTool (Toxicological data Reliability Assessment Tool) developed by the European Commission (https://eurl-ecvam.jrc.ec.europa.eu/about-ecvam/archive-publications/toxrtool). EPA implemented a literature search process for the first ten chemicals that included a comprehensive set of key words to capture as much of the literature for a given discipline as possible. However, even with a comprehensive literature search, some important studies may be missed. For instance, an abstract may not identify the chemical of interest by name (*e.g.,* if a genotoxicity test was conducted on many chemicals) and thus might be screened out from further consideration. In addition, some targeted searching for topics not anticipated at the beginning of the risk evaluation process (*e.g.,* generic inputs needed for an exposure model) might be needed. Therefore, such backwards searching (or snowballing) and targeted searching remain important aspects of the systematic review process. EPA will publish a protocol document for the next TSCA risk evaluations. Furthermore, EPA

		anticipates feedback from the NASEM TSCA Committee on its systematic review process and will carefully review their recommendations for the next 20 chemicals
Content/organization		
SACC	**SACC COMMENTS:** Recommendation: Add very concise summary tables that highlight previous hazard assessments and risk assessments (*e.g.,* EPA IRIS document, ATSDR, NTP, IARC, etc.) with their main conclusions. • For example, Section 1.3 on regulation and assessment history does not have enough detail in the main report and instead refers to other documents and Appendix A.	EPA references previous government assessments where relevant, however EPA decided not to add any additional tables containing results of other assessments to the main body in order to avoid further expansion of the large Risk Evaluation document.
SACC	**SACC COMMENTS:** Recommendation: One Committee member recommended adding the Global Harmonization System (GHS) classification to Section 1.1 on physical-chemical properties. • Including the GHS classification for the substance here as reference makes sense because this is the first description of the characteristics of the chemical. GHS classification provides a standardized way to look at the hazards across chemicals and is the most common way to communicate on hazards of chemicals to industrial users.	GHS classification has not been included in other finalized EPA Risk Evaluations. EPA will consider adding GSH classification to future Risk Evaluations.
SACC	**SACC COMMENTS:** Recommendation: Enhance Table 1-1 to include additional properties and property variability. The Committee had several comments on the physical-chemical properties in Table 1-1. Other properties should be added to the table, including properties related to dermal absorption (see Table 6 for dermal parameters recommended by the SACC for inclusion in the current and future TSCA risk evaluations). Include all properties that are used either explicitly or implicitly in modeling. Concern was expressed with the over-reliance on EPI Suite™, a tool that is no longer being supported (*e.g.,* the databases are not being updated). The	EPA has added dermal permeability parameters to Table 1-1 as recommended by the SACC. Other properties included are consistent with other Risk Evaluations.

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	variability associated with each property estimates should be included. Adding variability estimates allows for quantitative assessment of how this uncertainty impacts risk evaluation findings.	
SACC	**SACC COMMENTS:** Recommendation: Consider including a table or figure that shows mass balance information. The SACC recommended in previous assessments of TSCA chemical evaluations to include more information on the chemical manufacture, uses, and releases, which the Committee has referred to as the "mass balance" approach. This is a consolidation and expansion of several tables in the Problem Formulation, main report, and appendices. Committee members had differing opinions on the reasonableness of this approach and what it might entail. No consensus was reached on whether such a table would be useful or even able to be created. Problems with fulfilling the needs of a mass balance table include CBI, delays between manufacturing and use, and changing uses/formulations. The Committee recommended that EPA investigate possible solutions, such as using a multi-year average and aggregating information to avoid disclosure of CBI. Committee members provided Table 7 as one example of what a mass-balance table might look like. • One Committee member point out that the draft risk evaluation purported 2 million pounds of TCE lost. This is 2% of the total product volume and a mass balance approach would show where this loss is coming from. It would be a higher percentage if the loss came from the approximately 15% used to make TCE-containing products. • The estimates should also be updated for both the newer reports to EPA, as EPA has stated it will do, and for the market study. • Some Committee members commented that the TRI estimated releases are under-reported, while another Committee member commented that they are over-reported. The Committee agrees that TRI estimated releases are not accurate, although reporters try to report all their releases.	EPA's analysis uses TRI (U.S. EPA, 2017g) and DMR (U.S. EPA, 2016a) to estimate the highest local per site water releases of TCE. EPA has added a mass balance analysis as suggested to Appendix R of the Risk Evaluation.

SACC	**SACC COMMENTS:** Recommendation: Use figures instead of tables for production volume (Table 1-2) and uses (p. 42-43, lines 1659-1665). Sample figures were provided.	EPA has added figures for production volume and has removed the production volume tables.
SACC	**SACC COMMENTS:** Recommendation: Consider using table structures in the TSCA draft risk evaluation that are similar to those used in the associated IRIS assessment. In the draft risk evaluation, Tables 3-7 to 3-14 report dose-response analysis results for selected studies and present PODs, HECs, HEDs and Uncertainty Factor values used. In the 2011 TCE IRIS report (U.S. EPA, 2011b), Table 5-13 provides the same information but in a different format. In this case, the IRIS table is clearer. One Committee member strongly recommend the use of the IRIS report format for these tables, if for no other reason than for consistency.	EPA uses table structures consistent with the 2014 Workplan Risk Assessment of TCE, which EPA believes most succinctly and informatively presents endpoints under consideration for dose-response analysis.
SACC	**SACC COMMENTS:** Recommendation: Move exposure estimates based on workers central tendency exposures from Section 4 Risk Characterization to Section 2 Exposures. EPA chose to discuss ONUs' exposure estimates based on modeling or measurements in Section 2 – Exposures, but to discuss the central tendency exposure estimates based on workers in Section 4 – Risk Characterization. This is problematic because the estimates for ONUs based on workers are also exposure estimates, although with different levels of assumptions, uncertainty, and confidence. They should be included in Section 2 with the appropriate justification, description of uncertainties, caveats, etc.	EPA thanks the commenter for the recommendation. EPA will investigate the organization of exposure estimates and risk characterization discussions for future risk evaluations.
SACC	**SACC COMMENTS:** Recommendation: Provide more consistent and detailed discussion of PPE usage in the main draft risk evaluation document. PPE use is a critical issue that should have more information in the main document rather than referring the reader to the NIOSH memorandum. • Presentation of PPE issues in Section 2 is organized awkwardly.	EPA thanks the commenter for the recommendation. EPA has added a summary table (Table 4-9) presenting assumptions on respirator and glove usage for each OES. EPA will investigate the organization of exposure

	PPE for dermal exposures appears as part of subsection section 2.3.1.3.5 – Modeled Dermal Exposures, while for inhalation exposures it is presented in the next subsection, 2.3.1.3.5 – Consideration of Engineering Controls and Personal Protective Equipment, which discusses respirators, but inhalation exposures are described in Sections 2.3.1.2.1 through 2.3.1.2.4, well before dermal exposures. • Either the presentations of dermal and inhalation protection are made separately for each route of exposure in both cases, or there should be a separate subsection that discusses exposure controls and presents both types of PPE.	estimates and discussion of PPE for future risk evaluations.
SACC	**SACC COMMENTS:** Recommendation: Use the Department of Health and Human Services (DHHS) definition of adults consistently. Throughout the document, there is a need to be consistent and correct about the age cut-off for "adults." The draft risk evaluation should follow the DHHS guideline of adults being age ≥18 years. In some places, the draft risk evaluation uses either age 16 or 21 years as a cut-off; it is unclear why there is a lack of consistency. Page 186, lines 3128-3129 has a particularly odd definition of adults as age ≥11 years.	EPA has updated definitions and references throughout the document for consistency in defining adults vs. adolescents and children. The line in Section 2.3.3 has been clarified as referring to adults or children age 11 and up.
52	**PUBLIC COMMENTS:** It is notable that WOE is not addressed in the methods section of the draft risk evaluation (Section 1.5.3).	Section 1.5.3 of the TCE risk evaluation states "EPA considers quality, consistency, relevancy, coherence and biological plausibility to make final conclusions regarding the weight of the scientific evidence."
Presentation of uncertainty and conclusions		
SACC	**SACC COMMENTS:** Recommendation: Present uncertainty and confidence as in Table 2-26 throughout the draft risk evaluation. One Committee member commented they liked the presentation of uncertainty and overall confidence in a table format such as Table 2-26: Summary of overall confidence in inhalation exposure estimates by	These organizational comments are appreciated and will be considered in a revised template for the next round of chemicals to be evaluated under TSCA section 6.

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	OES. If the descriptions are systematized better, it would be a good model to follow for summarizing uncertainties and confidence throughout the risk evaluation, including summarizing PESS.	
Errors		
SACC	**SACC COMMENTS:** The dose levels in the Keil et al. (2009) study are misreported in the draft risk evaluation. They were 0.001, 0.4, or 14 ppm (0, 1, 400, or 14,000 ppb) TCE in water.	The dose levels used in the (Keil et al., 2009) study were not misreported. The dose levels stated by the commenter are actually misreported in the Abstract of the original publication, which presumably is the basis for the comment.
56	**PUBLIC COMMENTS:** Errors in Table 2-26: **Batch Open-Top Vapor Degreasing** • EPA states on p. 129: "These monitoring data include 123 data points from 16 sources, and the data quality ratings from systematic review for these data were ***medium***." • Based on the description on p. 705, the referenced data sources appear to be from these 10 studies: Daniels et al., 1988; Ruhe et al., 1981; Barsan, 1991; Ruhe, 1982; Rosensteel and Lucas, 1975; Seitz and Driscoll, 1989; Gorman et al., 1984; Gilles et al., 1977; Vandervort and Polakoff, 1973; and Lewis, 1980. • In the document "Systematic Review Supplemental File: Data Quality Evaluation of Environmental Releases and Occupational Exposure Data," all 10 studies received an overall quality determination of ***high***, not medium. **Spot Cleaning and Wipe Cleaning** • EPA states on p. 133: "These monitoring data include 8 data points from 2 sources, and the data quality ratings from systematic review for these data were ***medium***." • Based on the description on p. 732, the referenced data sources appear to be Burton and Monesterskey (1996) and NIOSH (1997). • In the document "Systematic Review Supplemental File: Data Quality Evaluation of Environmental Releases and Occupational	EPA agrees that the data quality ratings of the sources from systematic review were all scored as high. This has been corrected in the text. However, the overall confidence statements in Table 2-26 involve more than just the data quality. For the overall confidence statements, EPA considered the assessment approach, the quality of the data and models, and uncertainties in assessment results to determine an overall level of confidence. All these factors together yield an overall confidence factor of medium for the three occupational exposure scenarios (OES) described by the commenter. Additional description of how the overall confidence statements are determined is provided in the Appendix titled Data Integration Strategy for Occupational Exposure and Release Data/Information of the Supplemental Information on Releases and Occupational Exposure Assessment document.

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	Exposure Data," both Burton and Monesterskey (1996) and NIOSH (1997) received an overall quality determination of ***high*** (1.6 and 1.4, respectively; see p. 159 and 172 of the systematic review supplemental file), not medium. **Commercial Printing and Copying:** • EPA states on p. 134: "These monitoring data include ***20*** data points from 1 source, and the data quality ratings from systematic review for these data were ***medium***." • Based on the description on p. 737, the referenced data source appears to be Finely and Page (2005). • In the document, "Systematic Review Supplemental File: Data Quality Evaluation of Environmental Releases and Occupational Exposure Data," Finely and Page (2005) received an overall quality determination of ***high*** (1.6) and had 23 samples (see p. 126 of the systematic review supplemental file), not medium.	
96	**PUBLIC COMMENTS:** Table_Apx C-1 is incorrect: • The Occidental Chemical Corporation, Wichita, KS NPDES: KS0096903 facility does not release TCE to surface water or to a POTW (off-site wastewater treatment). All process wastewater and stormwater that falls on process areas is collected and disposed to a permitted deepwell system. TCE is a constituent detected in remediation extraction wells located on the manufacturing site; thus, any TCE waste resulting from extraction activities is disposed in the deepwell system. • The Occidental Chemical Corporation, Niagara Plant, Niagara Falls, NY NPDES: NY0003336 facility does not use TCE as an industrial processing aid. TCE is not used as an industrial process aid at the facility; TCE measured, if any, is from legacy disposal remediation at the site. • The Oxy Vinyls LP – Deer Park PVC, Deer Park, TX NPDES: TX0007412 facility does not use TCE in other industrial uses. TCE measured, if any, is from legacy remediation at the site.	Based on re-evaluation of TRI and DMR data, EPA has revised the Risk Evaluation to indicate the Occidental Chemical Corporation facility in Wichita, KS does not release TCE to surface water or off-site wastewater treatment. The SIC for the Occidental Chemical Corporation Niagara Plant reported in DMR (SIC 2812) (U.S. EPA, 2016a) translates to a NAICS code of 325180. This facility has been grouped with other facilities with the same/similar NAICS codes that have listed TCE use as an industrial processing aid in TRI. The TRI submission from the Oxy Vinyls LP facility in Deer Park, TX (U.S. EPA, 2017g) indicates "Ancillary of other use of TCE" which

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		EPA classified under the Other Industrial Use OES.
96	**PUBLIC COMMENTS:** Table_Apx E-3 is incorrect: The Occidental Chemical Corp, Wichita, Wichita KS NPDES: KS0096903 facility does not release TCE to surface water or to a POTW. Any TCE waste resulting from our remediation extraction activities is disposed in the deepwell system.	The comment is noted and this surface water release was removed from final risk evaluation.
96	**PUBLIC COMMENTS:** Table_Apx E-3 is incorrect: The Oxy Vinyls LP – Deer Park PVC, Deer Park, TX NPDES: TX0007412 facility does not use TCE in other industrial uses. TCE measured, if any, is from legacy disposal remediation at the site.	The TRI submission from the Oxy Vinyls LP facility in Deer Park, TX indicates "Ancillary of other use of TCE" which EPA classified under the Other Industrial Use OES.
96	**PUBLIC COMMENTS:** Table_Apx E-3 is incorrect: The Occidental Chemical Corp, Niagara Plant, Niagara Falls, NY NPDES: NY0003336 facility does not use OES as an industrial processing aid. TCE is not used as an industrial process aid at the facility; TCE measured, if any, is from legacy disposal remediation at the site.	The SIC for the Occidental Chemical Corporation Niagara Plant reported in DMR (SIC 2812) (U.S. EPA, 2016a) translates to a NAICS code of 325180. This facility has been grouped with other facilities with the same/similar NAICS codes that have listed TCE use as an industrial processing aid in TRI.
96	**PUBLIC COMMENTS:** • Table_Apx I-3 is incorrect: The Occidental Chemical Corp, Wichita, Wichita KS does not produce TCE in the annual volume at or greater than the production volume listed in Table_ApxI-3. The daily production volume in the table is also inaccurate and is greater than actual daily production values. Finally, there are no wastewater flows to surface water or a POTW from the site that contain TCE. • Table_Apx P-4 is incorrect: The Occidental Chemical Corp, Wichita, Wichita KS does not produce TCE at or greater than the annual or daily production volume listed in Table_Apx-P-4. There are no wastewater flows to surface water or a POTW from the site that contain TCE so the maximum, average, and annual release	The 2015 annual production volumes in the 2016 CDR (U.S. EPA, 2016c) for this site was either claimed as CBI or withheld. EPA estimated the production volume by subtracting known site production volumes from the national production volume and averaging the result over all the sites with CBI or withheld production volumes and converting from pounds to kilograms. The SIC for the Occidental Chemical Corporation Niagara Plant reported in DMR (SIC 2812) (U.S.

	columns should be zero (0). • Table_Apx P-30 is incorrect: The Occidental Chemical Corp, Niagara Plant, Niagara Falls, NY NPDES: NY0003336 facility does not use OES as an industrial processing aid. TCE is not used as an industrial process aid at the facility; TCE measured, if any, is from legacy disposal remediation at the site.	EPA, 2016a) translates to a NAICS code of 325180. This facility has been grouped with other facilities with the same/similar NAICS codes that have listed TCE use as an industrial processing aid in TRI.
Editorial comments		
SACC	**SACC COMMENTS:** General: • All references to documents should also include a link to the appropriate record in the EPA HERO database. • Be mindful to use the proper number of significant figures. • There are problems with formats in several tables. • Add a footnote to tables listing HE and CT indicating what they mean. • Acronyms and labels used in the draft risk evaluation should be sufficiently long and distinct enough to perform searches: acronyms such as "E1" and "E3" are insufficient. • Use the word "sex" instead of "gender," since sex refers to biological difference whereas gender is a social construct.	Supplemental document references are now all linked to the docket where they are contained. Significant figures have been reviewed, however inconsistencies in significant figures result from a preference for providing additional clarity when presenting values that can differ by several orders of magnitude. EPA has corrected any problematic formats in tables; HE = high-end, CT= central tendency. EPA attempts to use acronyms that are consistent throughout the document and with other Risk Evaluations. "Gender" has been changed to "sex" throughout the document.
SACC	**SACC COMMENTS:** Specific: • Pages 115-116, lines 1250-1256: provide citations to OSHA and NIOSH hierarchy of exposure controls. • Page 119: protect workers from exposure; line 1354 add citations. • Page 119, lines 1359-1361: something is missing in the sentence, suggest alternative with commas: "Respirator selection provisions are provided in § 1910.134(d) and require that appropriate respirators are (be) selected based on the respiratory hazard(s) to which the worker will be exposed, and (including) workplace and user factors that affect respirator performance and reliability." • Page 120, line 1371: provide the reference to the ACGIH TLVs, not to ATDSR, which is a secondary source. Unclear why primary	Citations have been added to the document as requested. The text has been revised accordingly to fix any errors. For page 259, EPA has added clarifying language to indicate whether toxicity values are EC_{50}s, LC_{50}s or NOECs or LOECs. As mentioned earlier, EPA derived the geometric mean, because the hazard values for all three species were similar, and because EPA had more

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	sources of information or data are sometimes not used. • Page 240, line 2110: "kidney" needs to be changed to "liver." • Page 259, lines 25-26 states: "For acute exposures to invertebrates, toxicity values ranged from 7.8 to 33.85 mg/L (integrated into a geometric mean of 16 mg/L). For chronic exposures, toxicity values for fish and aquatic invertebrates were as low as 7.88 mg/L and 9.2 mg/L, respectively." The Committee was uncertain as to what these values are. Are they median lethality values? EC_{50}s? NOAELs? LOAELs? What is the justification for using a geometric mean? The second sentence discusses chronic values for fish and invertebrates; what do these values represent? • Figures in Appendix F are captioned as "tables."	confidence in a COC derived from a geometric mean for three species than a COC derived from one value from one species. EPA added a justification for using the geometric mean in calculating an acute COC in the 3.1.5 Section of the Risk Evaluation.
SACC	**SACC COMMENTS:** Recommendations: (1) Modify Tables 2-7, 2-8, and 2-9 to make it clear they refer to estimated concentrations. (2) Modify Table 2-2 to clarify that it applies to water releases. • A Committee member had difficulty finding an estimate of the total pounds of TCE released to waterways. The problem formulation lists 52 pounds for 2015 (Problem Formulation, p. 31 Table 2-7, U.S. EPA, 2018). Later in that document, there is a release value from DMR data of 1,564 pounds (p. 34, Section 2.3.4). • The Committee recommended that EPA make it clear that Table 2-7, 2-8, and 2-9 present estimated aqueous concentrations. Table titles and figure captions should "stand alone." The captions should better distinguish between estimated and measured aqueous concentrations. Similarly, it is not clear that Table 2-2 refers to water releases. Additional comments on Table 2-2 and associated text noted by members: • Estimated daily releases per COU depend heavily on TRI and DMR data for 2016 and assumes 260 days of operation per year. • Impact on TRI data comes only from those manufacturers/ processors having 10 full-time employees, and that handle greater	Regarding the recommendations, (1) The three table titles have been edited as recommended, (2) Table 2-2 has been updated to clarify that it refers to water releases. The total mass of TCE released to water was not presented as EPA's analysis uses TRI (U.S. EPA, 2017g) and DMR (U.S. EPA, 2016a) to estimate the highest local per site water releases of TCE. The assumptions and uncertainties associated with using TRI and DMR data sources are discussed in Section 2.2.2.3 and Section 4.3.

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	than 25,000 pounds (manufacturers) or 10,000 pounds (processors). • Impact on DMR data of requirement to load major discharger data, but optional to load minor discharger data, and the fact that distinction between major/minor is set independently by each state.	
SACC	**SACC COMMENTS:** Recommendation: Correct issues with Figure 3-1. • The green algae *Raphidocelis subcapitata* is formally called *Pseudokirchneriella subcapitata*. In the environmental hazard data extraction table for TCE (U.S. EPA, 2020b), the label *Pseudokirchneriella subcapitata* is used. In Figure 3-1, the newer name *Raphidocelis subcapitata* is used. The Committee suggested using the most recent taxonomic nomenclature consistently throughout. • The green algae (*Raphidocelis subcapitata*) has a toxicity value from the Data Extraction Table of log10(411.5) = 2.61 [Medium quality (Lubra et al., 2010) and high quality (Tsai and Chen, 2007)] whereas in Figure 3-1, the toxicity value for *Raphidocelis subcapitata* is shown at a value below 2. • Value for the diatom (*Skeletonema costatum*) in Figure 3-1 is below 2, whereas the value should be log10(122.5) = 2.088 [Medium quality (Ward et al., 1986)]. • The value for green algae (*Parachlorella kessleri*) in Figure 3-1 at toxicity value of log10(640) = 2.8 [Medium quality (Lukavsky et al., 2011)] is not included in the figure. • The value for the green algae (*Chlamydomonas reinhardtii*) in Figure 3-1 at a toxicity value of log10(24.4) = 1.39 [High quality 72-hour (Brack and Rottler, 1994)] is not included in the figure. Other specific comments: • Genus previously *Rana* is now *Lithobates* (draft risk evaluation p. 190, lines 9293 and throughout). • Also note that developmental effects could result in premature mortality in these aquatic organisms (p. 191, lines 98-102). • Please be specific regarding the term "mild intoxication." If this is	Scientific name updates have been made in their respective sections. EPA double checked on the toxicity values listed in Figure 3-1. Some values were used because they were either more relevant or of higher quality than others. Each toxicity value used in the SSDs were listed in Appendix E1 for full transparency. A mention of developmental effects potentially resulting in premature death was added to Section 3.1.2. In terms of describing "mild intoxication" further, the original study, Ward et al. (1986), did not specify what behaviors were included in this description.

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	narcosis or lethargy, please state as such (draft risk evaluation p. 192, line 144).	
56, 108	**PUBLIC COMMENTS:** The scheme used to calculate the overall rating for a particular study is not clearly presented in either the updated criteria document or the draft risk evaluation. For the following equation, the subscripts of *i* and *j* are not defined, and the final subscript of *0.1* is not explained. From this description, it is not possible to see how EPA OPPT calculated its overall ratings. [illegible]	EPA's systematic review is currently based on *Application of Systematic Review in TSCA Risk Evaluations*. Revisions to systematic review are under development (*Systematic Review Protocol Supporting the TSCA Risk Evaluations*); EPA anticipates feedback from the NASEM TSCA Committee on its systematic review process, including the epidemiological data quality criteria, and will carefully review and implement relevant recommendations.
94	**PUBLIC COMMENTS:** In the text: "contrasts within the study population and were either 1) comparisons of groups exposed and not exposed to [TCE]..," there appears to be a typographical error, because the sentence refers to perchloroethylene instead of TCE.	EPA appreciates the commenter pointing out this error. The paragraph should refer to TCE, not perchloroethylene.
Miscellaneous		
31	**PUBLIC COMMENTS:** Restriction of such a substance would be in violation of free-trade, and could therefore pose, an unmitigated threat to our capitalist society. As such, TCE should be allowed as an intermediate in the process of manufacturing hydrofluorocarbon HFC-134a.	Thank you for your comment. Per 15 U.S.C § 2605, EPA is required to prioritize, evaluate and manage unreasonable risks of chemical substances and mixtures.
35	**PUBLIC COMMENTS:** Why isn't there any mention of fetal heart defects or warnings for pregnant women? There should be warnings. We don't want to cause birth defects unknowingly.	
89	**PUBLIC COMMENTS:** The petro-chemical industry has a vested interest in seeing the allowable levels of TCE made very high; banning of TCE would require	

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	finding an alternative to this very powerful (and very toxic) chemical. We cannot continue to put the interests of the petro-chemical industry ahead of the value of human lives. Please maintain stricter levels of presence of TCE in ground and drinking water, vapor intrusion levels, and dermal contact.	