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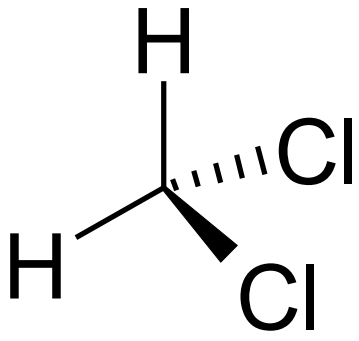
Office of Chemical Safety and
Pollution Prevention

Summary of External Peer Review and Public Comments and Disposition for Methylene Chloride (MC)

Response to Support Risk Evaluation of Methylene Chloride (MC)



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EPA published the Draft Risk Evaluation for Methylene Chloride (Dichloromethane, DCM) in October of 2019, and accepted public comments until December 30, 2019. Materials on the draft risk evaluation are available at www.regulations.gov in docket EPA-HQ-OPPT-2019-0437. EPA held a peer review meeting of EPA's Science Advisory Committee on Chemicals (SACC) on the draft risk evaluation for this chemical's conditions of use on December 3-4, 2019.

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

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

The peer review and public comments are categorized by the MC peer review charge questions, which align with the seven themes listed below. Additionally, within each theme comments that cover similar issues are presented together.

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

ABBREVIATIONS

1-BP	1-Bromopropane
ACC	American Chemistry Council
ACE	Acute-to-Chronic Estimation
ADC	Average daily concentration
AF	Assessment factor
AFL-CIO	American Federation of Labor and Congress of Industrial Organizations
AEGL	Acute Exposure Level Guidelines
AIHA	American Industrial Hygiene Association
AOP	Adverse outcome pathway
APF	Assigned protection factor
APHA	American Public Health Association
APHL	Association of Public Health Laboratories
AQMD	Air Quality Management District
ASD	Autism Spectrum Disorder
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	Bioconcentration Factor
BMDL	Benchmark dose lower bound
BMDS	Benchmark Dose Software
BW	Bodyweight

CAA	Clean Air Act
CalEPA	California Environmental Protection Agency
CASRN	Chemical Abstracts Service Registry Number
CEM	Consumer Exposure Model
COU	Condition of use
CFD	Computational fluid dynamics
ChV	Chronic value
CNS	Central Nervous System
COC	Concentration of concern
CWA	Clean Water Act
DMR	Discharge Monitoring Report
EC_{50}	Effect Concentration at which 10% of test organisms exhibit the effect
ECEL	Existing Chemical Concentration Limit
EDF	Environmental Defense Fund
E-FAST	Exposure and Fate Assessment Screening Tool
EIA	Environmental Investigation Agency
EPI Suite™	Estimation Programs Interface suite of models
EPN	Environmental Protection Network
EXAMS	Exposure Analysis Modeling System
GHS	Globally Harmonized System
GST	Glutathione S-transferase T1-1
HAP	Hazardous air pollutant
HBCD	Cyclic aliphatic bromide cluster
HEC	Human equivalent concentration
HEI	Health Effects Institute
HERO	Health & Environmental Research Online
HSIA	Halogenated Solvents Industry Alliance
HUC	Hydrologic unit code
IARC	International Agency for Research on Cancer
IUR	Inhalation unit risk
K_{oa}	Octanol-Air Partition Coefficient
K_{oc}	Soil Organic Carbon-Water Partitioning Coefficient
LADC	Lifetime average daily concentrations
LC_{01}	Lethal Concentration at which 1% of test organisms die
LC_{10}	Lethal Concentration at which 10% of test organisms die
LC_{50}	Lethal Concentration at which 50% of test organisms die
LOAEL	Lowest Observed Adverse Effect Level
LOD	Limit of detection
MC	Methylene chloride
MOA	Mode of Action
MOE	Margin of Exposure
NAICS	North American Industry Classification System
NAS	National Academies of Science
NATA	National Air Toxics Assessment
NEI	National Emissions Inventory
NESHAP	National Emission Standards for Hazardous Air Pollutants

NF	Near-field
NHANES	National Health and Nutrition Examination Survey
NIOSH	National Institute for Occupational Safety and Health
NMP	N-Methylpyrrolidone
NOAEL	No Observed Adverse Effect Level
NOEC	No Observed Effect Concentration
NPDES	National Pollutant Discharge Elimination System
NTP	National Toxicology Program
OECD	Organisation for Economic Co-operation and Development
OES	Occupational exposure scenario
OPERA	Open Structure-activity/property Relationship App
OPPT	Office of Pollution Prevention and Toxics
ONU	Occupational non-user
OSHA	Occupational Safety and Health Administration
PBPK	Physiologically based pharmacokinetic
PEL	Permissible exposure limits
PDM	Probabilistic Dilution Model
PF	Protection factor
POD	Point of departure
POTW	Publicly owned treatment works
PPE	Personal protective equipment
QSAR	Quantitative Structure-Activity Relationship
REL	Reference Exposure Level
RIOPA	Relationship between Indoor, Outdoor, and Personal Air
ROS	Regression on Order Statistics
RQ	Risk quotient
SACC	Science Advisory Committee on Chemicals
SCHF	Safer Chemicals Healthy Families
SDS	Safety Data Sheet
SIR	Standard incidence rates
SOCMA	Society of Chemical Manufacturers & Affiliates
STORET	STOrage and RETrieval database
TNO	The Netherlands Organisation for Applied Scientific Research
TRI	Toxics Release Inventory
TSCA	Toxic Substances Control Act
TURI	Toxics Use Reduction Institute
TWA	Time-weighted average
UCSF PRHE	University of California, San Francisco Program on Reproductive Health and the Environment
UF	Uncertainty factor
U.S. BLS	United States Bureau of Labor Statistics
USGS	U.S. Geological Survey
VOC	Volatile organic compound
WASP	Water Quality Analysis Simulation Program
WHO	World Health Organization
WOE	Weight-of-evidence

List of Comments		
#	**Docket File**	**Submitter**
SACC	N/A	Science Advisory Committee on Chemicals (SACC)
28	EPA-HQ-OPPT-2019-0437-0028	Tamara Fox, Vertex Pharmaceuticals, Inc.
33	EPA-HQ-OPPT-2019-0437-0033	Mass Comment Campaign sponsored by Environmental Defense Fund (EDF) (web)
34	EPA-HQ-OPPT-2019-0437-0034	Melvin Andersen, Andersen ToxConsulting LLC
41	EPA-HQ-OPPT-2019-0437-0041	Suzanne Hartigan, Senior Director, Regulatory and Technical Affairs, American Chemistry Council (ACC)
42	EPA-HQ-OPPT-2019-0437-0042	Richard A. Denison, Lead Senior Scientist, Environmental Defense Fund (EDF)
43	EPA-HQ-OPPT-2019-0437-0043	Sebastian Irby, Environmental Protection Network (EPN)
44	EPA-HQ-OPPT-2019-0437-0044	Bob Sussman, Counsel, Safer Chemicals Healthy Families (SCHF)
45	EPA-HQ-OPPT-2019-0437-0045	Andrew Maier, Senior Managing Health Scientist, Cardno ChemRisk
46	EPA-HQ-OPPT-2019-0437-0046	Kenneth A. Mundt, Senior Principal Health Scientist, Cardno ChemRisk
47	EPA-HQ-OPPT-2019-0437-0047	Anonymous
48	EPA-HQ-OPPT-2019-0437-0048	Laura Reinhard, Vice President and General Manager, Foam and Industrial Products, Honeywell
49	EPA-HQ-OPPT-2019-0437-0049	Jonathan Kalmuss-Katz, Staff Attorney, Earthjustice
50	EPA-HQ-OPPT-2019-0437-0050	Richard A. Denison, Lead Senior Scientist, Environmental Defense Fund (EDF) (Attachment to OPPT-2019-0437-0042)
51	EPA-HQ-OPPT-2019-0437-0051	Gustav A. Ruggiero, Johnson Matthey Inc. (JMI)
52	EPA-HQ-OPPT-2019-0437-0052	Eric Kendall, R&D Director, Adhesives Division, Wilsonart LLC
53	EPA-HQ-OPPT-2019-0437-0053	W. A. Chiu
54	EPA-HQ-OPPT-2019-0437-0054	Bob Sussman, Counsel, Safer Chemicals Healthy Families (SCHF)
55	EPA-HQ-OPPT-2019-0437-0055	Jennifer Sass, Senior Scientist, Natural Resources Defense Council (NRDC)
56	EPA-HQ-OPPT-2019-0437-0056	Suzanne Hartigan, Senior Director, Regulatory and Technical Affairs Department, American Chemistry Council (ACC)
57	EPA-HQ-OPPT-2019-0437-0057	Penelope Fenner-Crisp, Environmental Protection Network (EPN)
58	EPA-HQ-OPPT-2019-0437-0058	Tracey Woodruff, Professor and Director, Program on Reproductive Health and the Environment, School of Medicine, University of California, San Francisco
59	EPA-HQ-OPPT-2019-0437-0059	Melvin E. Andersen, Andersen ToxConsulting, LLC

List of Comments		
#	**Docket File**	**Submitter**
60	EPA-HQ-OPPT-2019-0437-0060	Julia M. Rege, Senior Director, Environment & Energy, Association of Global Automakers, Inc
61	EPA-HQ-OPPT-2019-0437-0061	Mass Comment Campaign sponsored by Environmental Defense Fund (EDF)
62	EPA-HQ-OPPT-2019-0437-0062	Christina Starr, Environmental Investigation Agency (EIA)
63	EPA-HQ-OPPT-2019-0437-0063	Eric Berg, Deputy Chief, California Division of Occupational Safety and Health (Cal/OSHA)
64	EPA-HQ-OPPT-2019-0437-0064	Philip M. Fine, Deputy Executive Officer, Planning, Rule Development & Area Sources, South Coast Air Quality Management District (AQMD)
65	EPA-HQ-OPPT-2019-0437-0065	Jared Rothstein, Senior Manager, Regulatory Affairs, Society of Chemical Manufacturers & Affiliates (SOCMA)
66	EPA-HQ-OPPT-2019-0437-0066	S. Abbott et al.
67	EPA-HQ-OPPT-2019-0437-0067	Faye Graul, Executive Director, Halogenated Solvents Industry Alliance, Inc. (HSIA)
68	EPA-HQ-OPPT-2019-0437-0068	Suzanne Hartigan, Senior Director, Regulatory and Technical Affairs, American Chemistry Council (ACC)
69	EPA-HQ-OPPT-2019-0437-0069	Swati Rayasam, Science Associate, Program on Reproductive Health and the Environment, University of California, San Francisco (UCSF PRHE) et al.
70	EPA-HQ-OPPT-2019-0437-0070	Massachusetts Toxics Use Reduction Institute (TURI)
71	EPA-HQ-OPPT-2019-0437-0071	Georges C. Benjamin, Executive Director, American Public Health Association (APHA)
72	EPA-HQ-OPPT-2019-0437-0072	Randy Rabinowitz, Executive Director, Occupational Safety & Health Law Project and Jonathan Kalmuss-Katz, Staff Attorney, Earthjustice on behalf of American Federation of Labor and Congress of Industrial Organizations (AFL-CIO) et al.
73	EPA-HQ-OPPT-2019-0437-0073	Stephanie Schwarz, Legal Fellow, Environmental Defense Fund (EDF)
74	EPA-HQ-OPPT-2019-0437-0074	Randy Rabinowitz, Executive Director, Occupational Safety & Health Law Project and Jonathan Kalmuss-Katz, Staff Attorney, Earthjustice on behalf of American Federation of Labor and Congress of Industrial Organizations (AFL-CIO) et al. (Exhibits to OPPT-2019-0437-0072)

List of Comments		
#	**Docket File**	**Submitter**
75	EPA-HQ-OPPT-2019-0437-0075	Liz Hitchcock, Director, Safer Chemicals Healthy Families (SCHF) et al.
76	EPA-HQ-OPPT-2019-0437-0076	Letitia James, Attorney General of New York et al.
77	EPA-HQ-OPPT-2019-0437-0077	Amy McCamphill, Senior Counsel and Amy Chyao, Assistant Corporation Counsel, Environmental Division, Law Department, City of New York
79	EPA-HQ-OPPT-2019-0437-0079	Anonymous

Environmental Fate and Exposure		
EPA qualitatively analyzed the sediment, land application, and biosolids pathways based on methylene chloride's physical/chemical and fate properties. Exposure estimates to the environment were developed for the conditions of use for exposures to aquatic organisms. **Charge Question 1.1.** Please comment on EPA's qualitative analysis of pathways based on physical/chemical and fate properties. **Charge Question 1.2.** Please comment on the data, approaches and/or methods used to characterize exposure to aquatic receptors.		
#	**Summary of Comments for Specific Issues Related to Charge Question 1**	**EPA Response**
Need to describe in more detail the selection of environmental pathways and receptors		
SACC	**SACC COMMENTS:** • Clarify to what extent excluded environmental pathways (e.g., groundwater, soil) are addressed by other regulations and add this information to the conceptual model (Figure 2-1). • Clarify why no terrestrial pathways and receptors were considered, especially since soil discharges were at least as likely as discharges via publicly owned treatment works (POTWs).	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. Emissions to ambient air from commercial and industrial stationary sources, and associated inhalation exposures of terrestrial species, are under the jurisdiction of of the Clean Air Act (CAA), Safe Drinking Water Act (SDWA), Clean Water Act (CWA), and Resource Conservation and Recovery Act (RCRA). 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 conducted a screening level analysis to consider whether pathways of exposure for terrestrial organisms should be further analyzed and determined that terrestrial organism exposures to MC was not of concern partially based on estimates of soil concentrations several orders of magnitude below concentrations observed to cause effects in terrestrial organisms. In addition, methylene chloride is not expected to bioaccumulate in tissues, and concentrations will not increase from prey to predator in either aquatic or terrestrial food webs. This language was brought forward to discussion of conceptual model in risk evaluation.
Additional environmental pathways and receptors that should be considered		

MC RESPONSE TO COMMENT

SACC	**SACC COMMENTS:** • Seabirds may be impacted by MC volatilizing from surface waters near points of discharge. This pathway should be analyzed for risk.	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). MC 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 persistence in the atmosphere (photolysis half-life by OH• reaction = 79 days), MC 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 for risk, and EPA was able to assess risk based on qualitative analysis.
SACC, 70, 73	**SACC AND PUBLIC COMMENTS:** • EPA omits consideration of a number of possible sources of MC exposure. MC is present in air, soil, and sediment and will likely expose terrestrial and sediment-dwelling organisms. EPA noted that MC was found in 20% of sediment samples in the STORET database (p. 26, Problem Formulation). The rationale for not considering exposures to sediment-dwelling organisms is unclear. The risk evaluation states that MC in sediment is expected to be in the porewater rather than sorbed to the sediment organic matter. However, the log Koc of 1.4 indicates that the concentration in sediment organic matter will be 25 times higher than porewater (without considering volatilization or sediment degradation rates).	Clarifying language about what pathways are addressed under other statutes has been added to Section 1.4.2 of the Risk Evaluation. Additionally, the STORET data showing detections in 20% of samples was summarized by Staples et al., 1985, and quoted by ATSDR (https://www.atsdr.cdc.gov/toxprofiles/tp14.pdf). Staples et al. stated that the median concentration measured in sediment was 13 µg/kg, equivalent to 13 ppb, which is more than 2 orders of magnitude below the chronic (1,800 ppb) and acute concentration of concern (COC) (36,000 ppb) values estimated for sediment invertebrates by read-across from COCs reported for aquatic invertebrates. Although the log K_{OC} indicates that MC 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 equal to or less than 3.8, indicating that at equilibrium, concentrations in sediment would be expected to be less than four 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 MC 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).
54, 73	**PUBLIC COMMENTS:** • EPA disregarded pathways of exposure to sediment and terrestrial organisms based on estimated partition coefficients that assume that chemical equilibrium has been established. However, chemicals of concern can occur in high concentrations in different environmental compartments prior to reaching equilibrium. A better approximation approach might be the Level III Fugacity model, as suggested by the SACC, which predicts that 11% of MC will be distributed to soil, 44.1% to air, 44.8% to water, and the remainder (0.13%) to sediment, as calculated using EPI Suite 4.11. An 11% distribution to soil cannot be dismissed as de minimis. • Because of its high volatility and use as a solvent in many open operations, a large fraction of the total amount of MC produced is lost to the atmosphere. Estimates of total emissions are high and MC has been widely found in ambient air. SACC has previously criticized EPA's failure to include all environmental exposure pathways in its determinations of health risk, and the MC	• During problem formulation EPA conducted a screening level analysis to consider whether pathways of exposure for sediment and terrestrial organisms should be further analyzed and determined that terrestrial organism exposures to MC was not of concern partially based on estimates of soil concentrations being several orders of magnitude below concentrations observed to cause effects in terrestrial organisms. See prior response for more information on the sediment pathway. • EPA did not include the emission pathways to ambient air from commercial and industrial stationary sources, because releases of methylene chloride from stationary source to ambient air are under the jurisdiction of and addressed by Section 112 of the Clean Air Act (CAA). Resulting exposure were out of scope as described in the problem formulation for MC. Clarifying language about what pathways are addressed under other statutes has been added to Section 1.4.2 of the Risk Evaluation. Spills/leaks • Spills and leaks generally are not included within the scope of a TSCA risk evaluation. EPA is exercising its authority under

	evaluation has the same weakness. The contribution of air emissions to total should be accounted for, particularly in areas near emitting facilities, and should be combined with other routes of exposure. • Due to its high volatility, MC spills and leaks will likely lead to soil vapor intrusion as a potential exposure pathway. This pathway should be considered but was not addressed in the draft risk evaluation. • In addition to the fact that several million pounds of MC are released annually into the air due to its volatility, disposal to water may also create a route of exposure to organisms living at the water-atmosphere interface (e.g., aquatic plants, amphibians, and/or shorebirds). These organisms may be disproportionally impacted by MC. In its literature review, EPA dismissed a study that not only identified a BCF of 577 in water moss (Thiebaud et al., 1994), but also found that concentrations at the water-atmosphere interface may be more significant than aquatic concentrations. • EPA unjustifiably disregarded Theibaud et al. (1994). According to the Systematic Review Supplemental File: Data Quality Evaluation of Environmental Hazard Studies, EPA determined the study to be of unacceptable quality, despite giving it a mean score of 1.5 (defined as "high" quality) because one metric, the outcome assessment methodology (Metric 17), was rated as "unacceptable" because, according to the comments, there was "[n]o adverse outcome. This study analyzed the bioaccumulation/ concentration factors of DCM" (p. 64). As such, this metric should have been rated as "not	TSCA to tailor the scope of the risk evaluation for MC, rather than evaluating activities which are determined not to be circumstances under which MC is intended, known or reasonably foreseen to be manufactured, processed, distributed, used, or disposed of, or environmental exposure pathways addressed by another EPA-administered statute and associated regulatory program. • First, EPA does not identify MC spills or leaks as "conditions of use." EPA does not consider MC spills or leaks to constitute circumstances under which MC 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 MC 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 MC could be considered part of the listed lifecycle stages of MC, EPA has "determined" that spills and leaks are not circumstances under which MC 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 to exclude MC spills and leaks from the scope of the MC 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

	applicable" because the study did not seek to determine whether there was a hazard outcome and should rather have been considered a study of the chemical's environmental fate and transport.	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, 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 MC 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 MC 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 MC to be COUs. • Second, even if MC 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, exclude certain activities that EPA has determined to be conditions of use 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...." The approach discussed in the Risk Evaluation Rule and applied in the problem formulation documents 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). • Following coordination with EPA's Office of Land and Emergency Management (OLEM), EPA has found that exposures of methylene chloride 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 methylene chloride as hazardous waste no. U080). As a result, EPA believes it is both reasonable and prudent to tailor the TSCA risk evaluation for methylene chloride 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. • Thiebaud et al. (1994) was evaluated in the Supplemental File: Data Quality Evaluation of Environmental Fate Studies with a "high" quality rating for its assessment of bioaccumulation potential. It has been incorporated into the fate narrative (Section 2.1.2). The study remains unacceptable for evaluating environmental hazards; it was incorrectly categorized in environmental hazards, as a hazard endpoint was not assessed, so there were no data to evaluate from a hazard perspective.
The draft risk evaluation ignores regulation under the Clean Water Act (CWA)		
68	**PUBLIC COMMENTS:** • The decision to evaluate risk to aquatic life of MC exposure doesn't account for the Office of Water's extensive and long-standing regulation of MC under the CWA and CWA's water quality criteria and standard setting processes. EPA OPPT should include in the draft risk evaluation a summary of any discussions with Office of Water related to this issue.	Communication and coordination between program offices within EPA occurs regularly on TSCA-related efforts. While EPA has recommended water quality criteria for protection of human health for MC (EPA-HQ-OW-2014-0135), it has not developed CWA section 304(a) recommended water quality criteria for the protection of aquatic life for MC. Therefore, EPA evaluated exposures and risks to aquatic life in this TSCA risk evaluation.
Need for tiered exposure assessment approach		
68	**PUBLIC COMMENTS:** • EPA needs a tiered approach to environmental exposure assessment. The agency should better explain and provide more transparency into its approach. EPA applied a number of conservatisms to its estimates of environmental exposures, and specifically, surface water concentrations. While this approach may suffice for screening-level assessments, it does not represent real world situations.	In response to comments received from the SACC and the public, EPA included additional analysis of surface water concentrations, for the 5 facilities that show risk in Section 4.1 (Environmental Risk Characterization). The analysis now includes modeling of all facilities with known releases of MC to surface water according to Toxics Release Inventory (TRI) and Discharge Monitoring Report (DMR) data. Any facilities that show risk then go through an additional analysis with surface water concentrations estimated using fugacity models in EPI Suite™, which take volatilization into account, and water body information from EXAMS. The results show that environmental conditions can produce a wide range of surface water concentrations; however, that range

		encompasses concentrations estimated in E-FAST. Given this variation, EPA found that E-FAST surface water concentrations best represent estimated concentrations evaluated in this risk evaluation may best represent concentrations found at the point of discharge. The farther from the facility, the more uncertainty, and the lower the confidence EPA has in the concentration.
Need to consider climate change impact on physical/chemical parameters		
49, 75	**PUBLIC COMMENTS:** • Climate change may influence choice of vapor pressure, water solubility, and air-water partition coefficients to use in an assessment. • To the extent that specific impacts of climate change are difficult to predict, EPA may account for that uncertainty via sensitivity analyses, use of a broader range of temperature-related assumptions, or additional uncertainty factors (UFs).	Generally, the predicted increases in atmospheric temperatures will not modify physical-chemical or fate properties sufficiently to impact the risk evaluation. Based on its vapor pressure (435 mmHg at 25°C) MC is expected to volatilize from dry surfaces. Increasing temperatures from standard test conditions at 25°C to 30°C would increase vapor pressure by approximately 20%, which would generally increase MC volatilization and shift MC from soil and other dry media compartments to the air. Water solubility would increase, but MC is soluble in water (13 g/L at 25°C). MC's enthalpy of solvation, needed to correct its air-water partition coefficient for an increase in temperature, is not readily available; thus, EPA cannot at this time assess how increasing temperatures will change air-water partitioning and whether it will increase volatilization from water to air.
Release of MC to the environment		
SACC	**SACC COMMENTS:** • In the statement "37.8 million pounds were treated," it is unclear what is meant by "treated." One Committee member was concerned that this uncertainty implies that some "treated" MC could eventually be released to the environment. • One Committee member indicated that the reported releases on p. 79 seem too low, unless significant unassessed releases occur through the atmosphere.	This reference, in the Problem Formulation document, refers to treatment of waste documented in the TRI data. In TRI treatment refers to waste containing MC that is treated for destruction on-site or is sent to a POTW or other off-site location for treatment for destruction. If waste is ultimately released to the environment, it would be reported to TRI as a release. EPA clarified in Section 2.2.3 (Summary of Water Release Assessment) that the magnitudes of annual per site releases are "of MC to water." Releases through the atmosphere are not assessed in this section.
Discharge flow data		
SACC	**SACC COMMENTS:**	

	• It is unclear how the hydrologic unit code (HUC) flow data are used, and the description of the numbers of facilities releasing to different HUCs is confusing. Specifically, it is unclear whether the total flow value used an estimate for the basin or was measured flow at the discharging facility. • It was suggested that geometric means should be used instead of arithmetic means as the appropriate descriptor.	The hydrologic unit codes are used as an organizing landscape unit of measure to see where known discharging facilities are co-located with known monitoring locations. For the purposes of this assessment, a HUC8 and HUC12 represent the proximate watershed areas of known releases. The HUC units themselves do not have specific flow values associated with them. The flow values used for estimating instream concentrations of MC represent stream reach specific 7Q10 values associated with the discharging facility (where possible through a NPDES permit) or averages across industry codes. Section 2.3.1 has been edited to make the use of HUC units clearer. With regard to geometric means or arithmetic means descriptors, if the commenter is referring to the flow values, the EFAST modeling program uses various flow metrics in its calculations including 7Q10s, harmonic means, 30Q5s and 1Q10s depending on the desired output. For surface water quality modeling, a 7Q10 flow value is typically used instead of a mean flow value since the EFAST model uses it as an input to calculate days of exceedance of an input concentration of concern for aquatic wildlife endpoints. Similarly, for drinking water exposures, a 30Q5 flow value is used.
Inconsistencies/errors in landfill or biosolids release assumptions		
SACC	**SACC COMMENTS:** • It is unclear whether biosolid application is the only route of discharge to the soil environment that can be considered under TSCA.	Typically, the primary release pathway directly to soil through land application of biosolids or as leachate from landfills. Landfills are under the jurisdiction of RCRA (see section 1.4.2 of the risk evaluation). Land application of biosolids is not covered under other statutes so it was included the scope of this risk evaluation.
49	**PUBLIC COMMENTS:** • "If methylene chloride is placed in a landfill or discharged to soil, it can seep into groundwater and contaminate nearby wells." MC has been detected in the soil and groundwater at numerous federal Superfund sites. In the draft risk	• Landfill exposures were not included in the environmental exposure conceptual model or assessed because disposal of methylene chloride via underground injection, RCRA Subtitle C hazardous waste landfills, RCRA Subtitle D municipal solid waste (MSW) landfills, and on-site releases to land from

	evaluation, however, EPA states that "[s]tudies clearly associated with releases from Superfund sites … and landfills were considered out of scope … and excluded from data evaluation and extraction." EPA also ignored available data on MC in leachate. • MC is present in biosolids from wastewater treatment, which are then applied to land as fertilizer. The MC risk evaluation should include an evaluation of available data that identify where these types of applications are made, numbers of people exposed, and presence/numbers of sensitive biological receptors exposed by this pathway.	industrial non-hazardous waste and construction/demolition waste landfills are covered under the jurisdiction of RCRA. • EPA qualitatively assessed discharges of MC in biosolids based on its physical chemical and fate properties. Based on its vapor pressure (435 mmHg at 25°C) and Henry's law constant (0.00291 atm-m^3/mole), MC in land-applied biosolids is expected to primarily volatilize to air, where it will disperse into the atmosphere. Additionally, 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). MC is not expected to bioaccumulate in tissues, and concentrations will not increase from prey to predator in either aquatic or terrestrial food webs.
Physical/chemical property and fate values and interpretation		
SACC	**SACC COMMENTS:** • Adding values for environmental partition coefficients and relative rates of transport and transformation to Figure 2-1 (p. 65) would provide a more quantitative description of the pathways. • Add octanol-air partition coefficient (Koa) values to the physical-chemical property table. • Henry's Law values should be reported as dimensionless air-water partition coefficients since partition coefficients directly relate chemical concentrations in the two phases that are in equilibrium. • Be more precise in how equilibrium properties are used to describe relative concentrations. For	The environmental fate diagram was updated with partition coefficients and degradation rates. The K_{OA} value reported in the PhysProp database in EPI Suite™ has been added to the physical chemical properties table. The Henry's law constants with the units atm-m^3/mol was converted to the dimensionless value and added to the p-chem properties table. The language of the risk evaluation has been modified to clarify the issue of equilibrium concentrations versus rates of transport or degradation. The quoted statement on biosolids was amended to read, "Based on the results of the Sewage Treatment Plant [STP]

	example, the risk evaluation states (p. 64): "Based on high volatilization, negligible adsorption, and possible biodegradation, concentrations of methylene chloride in land-applied biosolids are expected to be lower than concentrations in wastewater treatment plant effluents." This statement is true only if volatilization and/or biodegradation rates are rapid relative to sorption. • Review the risk evaluation for incorrect environmental fate statements associated with implied rates to equilibrium of physical-chemical properties. For example, equilibrium properties such as Henry's law and vapor pressure do not inform volatilization rates in the environment. Henry's law constant is an equilibrium value not a rate. • The photolysis process referred to in Table 2-1 should be clearly identified as "atmospheric oxidation via the OH radical." • The term 'sorption,' which includes both adsorption and absorption, is preferred over 'adsorption' when discussing the interaction of an organic chemical with an environmental solid (see review by Doucette, 2003). • The risk evaluation assumes that all sediment environments are anaerobic (e.g., p. 299). This is not likely to be true in many shallow, rapid flow rivers. • The following statement (p. 64) is incorrect: "Based on its vapor density (2.93 relative to air), volatilized methylene chloride is expected to remain near ground level." This would only be true for a very short period of time after release.	model, in which removal of methylene chloride from wastewater is dominated by volatilization, in combination with possible biodegradation, concentrations of methylene chloride in land-applied biosolids are expected to be lower than concentrations in wastewater treatment plant effluents." The risk evaluation document has been revised to avoid implying rates from Henry's Law constants (e.g., 'rapidly' was removed from the discussion of volatilization potential on pg 68 of the revised risk evaluation). However, it is noted that volatilization rates are controlled by resistances to mass transfer. In two-film theory, the mass-transfer coefficient associated with volatilization is directly related to the Henry's law constant. The suggested change has been made. The suggested change has been made throughout the document. The text has been edited to clarify that not all sediments are anaerobic. The text has been edited to specify that MC will remain near ground level in very calm conditions but disperse readily with mixing.

	At low concentrations and under most environmental conditions, MC would rapidly mix with air.	
66	**PUBLIC COMMENTS:** • There is a lack of clarity about inputs chosen for the modeling. For example, there was a high variation in the hydrolysis half-life value (Table 2-1); there is also an inconsistency in the standard temperature used.	The inputs for EPI Suite™ model runs are described in Appendix C of the risk evaluation. To summarize, the inputs were chemical name, CASRN number, and structure; and physical-chemical property values (water solubility, melting point, boiling point, log K_{OW}, vapor pressure, and Henry's law constant) as presented in Table 1-1 of the risk evaluation. Hydrolysis half-life (as presented in Table 2-1) was not entered as a model input in EPI Suite™.
73	**PUBLIC COMMENTS:** • In its assessment of biodegradation studies to understand fate and transport of MC through the environment, EPA states that "[s]ufficient numbers of high-confidence biodegradation studies were available" for this endpoint (p. 62). However, of the three aerobic biodegradation studies, one of the high-confidence studies cited by EPA indicates that for aerobic activated sludge there was 0% degradation of MC in 28 days, whereas a second study found 100% degradation in 7 days (Table 2-1, p. 63). According to the authors of the first study, MC is non-biodegradable and causes cellular lyses (Lapertot and Pulgarin, 2006). The second study, in contrast, showed rapid degradation (Tabek et al., 1981). The stark difference between the biodegradation rates reported in these studies is not examined further by EPA and is instead simply reported as having a range "depending on the microorganisms present and previous adaptation to methylene chloride" (p. 63). This is an important caveat; without proper microbial consortia and environmental conditions, biodegradation may not occur, stall out, or proceed slowly enough to expose receptors.	Discussion of this issue has been added to the fate uncertainties Section (2.1.3) and to the environmental exposure assessment uncertainties and assumptions section (4.4.1). As it relates to EFAST not taking into account fate parameters like biodegradation, language describing additional analysis and evaluation on the effect water depth, wind speed and water velocity played on the volatilization rate of MC from surface water was described and added to the evaluation. Not taking these fate parameters into account may lead to an over estimation of risk. However, in response to this comment and others, EPA included additional analysis of surface water concentrations, for the 5 facilities that showed risk in the environmental risk characterization section. The analysis now includes modeling of all facilities with known releases of MC to surface water according to TRI and DMR data. Any facilities with risk then go through an additional analysis with surface water concentrations estimated using higher tier fugacity models in EPI Suite™, which take volatilization into account, and information from EXAMS. The results show that environmental conditions can produce a wide range of surface water concentrations which encompasses concentrations estimated in E-FAST.

	• The agency used a conservative assumption of no biodegradation in its E-FAST modeling. This conservative assumption should be carried throughout the evaluation because, the potential of slow or minimal biodegradation of MC is important in other aspects of environmental fate and transport, beyond what may occur in wastewater treatment facilities.	
Data quality, variability and uncertainty for physical/chemical and fate properties		
SACC	**SACC COMMENTS:** • The Committee suggested expanding the discussion on data quality assessment. Generally, physical-chemical properties can be considered high in quality if experimentally measured (unless there are obvious procedural or analytical problems), medium in quality if derived from other experimental data or relationships (e.g., by algorithm), and low if determined by *in silico* models (e.g., quantitative structure property relationships [QSPRs]; Hansch et al., 1995). However, EPA rated the hydrolysis value from Dilling et al. (1975) as "low" in Table 2-1 (even though Dilling et al. 1975 is rated as "high" in the data quality evaluation supplemental file) while an estimated value was ranked "high." • The Committee suggested adding more discussion of variability in physical/chemical properties obtained from EPI Suite™ and other references. For example, the aerobic activated sludge biodegradation data (Table 2-1, p. 63) show variability. The values from Lapertot and	Different data quality evaluation metrics are used for experiments or models, because the metrics are designed to identify possible issues with specific aspects of the studies. Thus, the data quality ratings for experimental results are not directly comparable to those for model results. The data are selected for use based on a data integration exercise in which the assessor weighs the study types (experimental, modeling), details of the studies, and their overall data quality ratings. High-quality measured data are selected for use first, and if they are unavailable the assessor will choose from among estimated values and lower-quality measured data. The error in the Dilling et al., 1975 data quality rating has been corrected so that Table 2-1 and the supplemental file agree. Discussion of the range of reported biodegradation rates has been added to the fate uncertainties section (2.1.3). Regarding the variability of the Lapertot and Pulgarin (2006) results, study quality scores were assigned according to the criteria outlined in *Application of Systematic Review in TSCA Risk Evaluations* and without respect to the reported values themselves. The results of the EPI Suite™ BIOWIN models, which estimate biodegradation rates, were presented in the MC problem formulation and have been added to the fate section of the risk evaluation.

	Pulgarin (2006) were considered high quality, even though these results were highly variable. EPA should provide a short discussion of why the values were dissimilar and present an estimated value(s) for comparison. • For values estimated within EPI Suite™, EPA should identify the estimation method used, rank values based on the reliability of the estimation method and provide the rationale for selecting one estimation method over another. • EPA should incorporate a description of the uncertainty associated with the measured and estimated physical-chemical and fate properties into the draft risk assessment. Several Committee members suggested estimating confidence intervals around each property and conducting a sensitivity analysis to determine whether potential variability would significantly change the outcome of the qualitative pathway analysis.	The bioconcentration factor, log K_{OC}, and aerobic biodegradability were the only values estimated with EPI Suite™ for which the program contains multiple calculation techniques. In each of these cases, the various techniques estimated values similar enough to result in equivalent fate assessments. The result of each technique is now presented in Table 2-1 or in the fate discussion. The rate of aerobic biodegradation is the key area of uncertainty in the fate assessment for MC. 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 MC.
73	**PUBLIC COMMENTS:** • Physical-chemical property models in EPI Suite™ that were used to derive environmental fate characteristics (Table 2-1) lack transparency in performance and applicability.	EPI Suite™ has undergone peer review and the models contained in EPI Suite™ have been published in peer-reviewed journals as described in the EPI Suite™ documentation. The training set for each QSAR model is available for the user to assess applicability of a given input structure, and the performance of the models is summarized in the EPI Suite™ help files and in the relevant published articles (see https://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface#peer).

	• Henry's Law constant, provided in Table 1-1, which was sourced from the literature, is not the value that EPA used in its evaluation. Without explanation, EPA instead used the Henry's Law constant that was estimated using EPI Suite™ (see pp. 63, 299, Section 4.1.4 Risk Estimation for Terrestrial).	The inconsistencies have been corrected (Section 2.1.2, pg. 70; Section 4.2.4, pg. 354).
	• It is important to be judicious in sourcing physical-chemical property values, justify reliance on particular sources and address any variability and uncertainty associated with the values, including ramifications for conclusions regarding environmental fate. Many of the values presented in the draft risk evaluation (Table 1-1, p. 39) were sourced from textbooks, which are not original data. The quality of the studies (or models) and the underlying data must be evaluated before they are used in a risk evaluation.	The sources used to collect physical-chemical property data for MC were all subjected to data quality evaluations based on metrics presented in the *Application of Systematic Review in TSCA Risk Evaluations* document, and the full data quality assessments are presented in a supplemental file.
	• It is unclear why EPA did not use the newer, more transparent QSPR model, OPEn structure-activity/property Relationship App (OPERA), for its estimation of environmental fate characteristics. OPERA includes the reporting of a chemical-specific applicability domain and was built using a newer database of physical-chemical parameters.	OPERA-estimated values have been added to the discussion of fate characteristics where measured values were not available.
Other comments		
67	**PUBLIC COMMENTS:** • The risk evaluation for MC cannot be considered complete without assessing the toxicity and flammability risks of alternative products. MC-based paint remover products were developed and became dominant because of their effectiveness and because they are not flammable. The draft risk evaluation does not	Under TSCA section 6(b), EPA is required to determine whether a chemical substance presents unreasonable risks without consideration of costs or other non-risk factors. Consideration of technically and economically feasible alternative substances is a step that may occur as part of a potential risk management action developed pursuant to TSCA section 6(c)(2)(C). This type of analysis could be considered as part of a subsequent risk management action if unreasonable risk are determined and

	consider the significant health risks of alternatives (e.g., acetone, methanol, toluene) in confined spaces used in a similar manner to MC.	regulatory considerations are pursued.

Environmental Releases and Exposure		
EPA evaluated releases to water and aquatic exposures for conditions of use in industrial and commercial settings. EPA used Toxics Release Inventory (TRI) and Discharge Monitoring Report (DMR) data to provide a basis for estimating releases. EPA used these releases and associated inputs within EFAST 2014 to estimate instream chemical concentrations and days of exceedance. EPA also evaluated monitored values of methylene chloride in surface water and where possible compared those values to estimated release concentrations. **Charge Question 2.1:** Please comment on the approaches, models, and data used in the water release assessment including comparison to monitored data. **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 the Agency for conducting or refining the water release assessment and relation to monitored data.		
#	**Summary of Comments for Specific Issues Related to Charge Question 2**	**EPA/OPPT Response**
Use of E-FAST to predict surface water concentrations		
SACC	**SACC COMMENTS:** • The Committee considered comparisons between E-FAST-generated surface water concentrations and monitoring data as inappropriate since the model is not applicable for volatile compounds like MC. o Modeled values generated from E-FAST were as high as 17,000 µg/L, which is inconsistent with the highest measured concentration reported at 134 µg/L and most measured values around 5 µg/L or less. o Even if the model were applicable to MC, the number of samples collected was too small to draw definitive conclusions on possible associations between measured concentrations in surface water and predicted concentrations from facility releases.	• In response to comments received from the SACC and the public, EPA included additional analysis of surface water concentrations for the 5 facilities that indicated risk in the environmental risk characterization section. The analysis now includes modeling of all facilities with known releases of MC to surface water according to TRI and DMR data. Any facilities with indicated risk then went through an additional analysis with surface water concentrations estimated using higher tier fugacity models in EPI Suite™, which take volatilization into account, and information from EXAMS. The results show that environmental conditions can produce a wide range of surface water concentrations which encompasses concentrations estimated in E-FAST. • EPA agrees that the lack of colocation between monitored values of MC and estimated surface water concentrations

	• Modify the E-FAST model to include volatilization or use a more appropriate model for MC that incorporates volatilization, such as the EPA WASP model (Ambrose, 1987) or Exposure Analysis Modeling System (EXAMS). • Use surface water monitoring data available for other similar chlorinated volatile solvents having larger databases to evaluate models and model predictions. • At a minimum, the half-lives predicted in the EPI Suite™ program could be used to adjust the E-FAST predicted surface water concentrations.	from known releases for the majority of results makes it difficult to draw definitive conclusions and stated this in Section 2.3.2. Nevertheless, the evaluated monitoring data within the United States showed that the majority of samples were at non-detectable levels and those with detectable levels of MC were below identified COCs. • EPA appreciates the suggestion to do modeling across similar classes of chemicals to evaluate model performance and predictive ability and will entertain those suggestions for future risk evaluations. However, absent monitoring programs designed to measure these concentrations proximal to discharging facilities, the co-location of monitoring information with known facility releases is expected to be small thereby limiting model verification with actual monitored values.
41, 68	**PUBLIC COMMENTS:** • EPA used its E-FAST model to predict surface water concentrations at the TRI/DMR facilities based on facility-specific emissions and wastewater treatment removal. The PDM was used to predict the number of days a stream concentration may exceed the designated COC. It is unclear whether EPA used the dilution factor for the site-specific receiving water body or the national 7Q10 dilution factor, which is equivalent to 1.0. The SACC should consider whether EPA should be using the 7Q10 value for the facility-specific receiving water body associated with the facilities discharge, rather than the E-FAST PDM 7Q10 for dilution. o Surface water dilution estimates calculated using E-FAST for a still water body (i.e., bays, lakes, and estuaries) typically range from 1 (representing no dilution) to 200 (p. 82).	• Wherever possible, EPA used site specific 7Q10 flow metrics to estimate flows at waterbodies receiving known facility releases. For still water bodies, a dilution factor approach is applied since no available 7Q10 metric is available. If neither of these metrics are available a flow associated with the industry sector of the discharging facility was chosen to approximate the instream flow (p. 84 of draft). • The Long Beach facility does discharge into a tidal estuary and has a given dilution factor of 1 within the EFAST model (see *Supplemental File: Supplemental Information on Surface Water Exposure Assessment;* (EPA, 2019b)). The uncertainties and assumptions of these estimates are discussed in Section 4.3 and while the commenter may be correct that such a waterbody would lead to greater dilution, EPA used the best available science to evaluate this facility. There was no better estimate of possible dilution occurring within this specific

	However, these assumptions are unrealistically low and do not reflect the reality of the facilities evaluated. For example, the Long Beach Water Pollution Control Plant (New York; Table 4-1, p. 289) discharges into a tidal estuary of the southern Long Island Sound and is likely to experience significantly greater dilution than assumed. EPA should conduct a more realistic, site-specific analysis for the limited number of distinct facilities that appear to show unacceptable risk quotients.	waterbody that was found.
Use of a mass balance approach to estimate discharges to the environment		
SACC, 73	**SACC AND PUBLIC COMMENTS:** • The Committee recommended performing a mass balance analysis to describe the disposition of all of the MC produced or imported to its ultimate disposal, in order to provide a more realistic estimate of environmental discharges and to ensure that the risk evaluation addresses all major exposure opportunities. • EPA relies on the CDR and TRI to compile estimates of discharges, but there are limitations on both of those reporting schemes that result in an incomplete picture. In the case of MC, over 260 million pounds of MC are manufactured in or imported into the United States annually (p. 40), yet less than 3 million pounds of MC were identified as released to the air and less than 3,000 pounds to surface water. One Committee member suggested that using the National Emission Standards for Hazardous Air Pollutants (NESHAP) might be another approach to estimate releases to water since it contains purchase records, disposal records and air releases. The remainder could be interpreted as releases to water.	• EPA does not have reasonably available mass balance data to conduct such an analysis for MC. EPA's analysis uses TRI and DMR to estimate the highest local per site water releases of MC. • NESHAPs are air regulations that require companies to keep certain records; however, these records are retained by individual sites and companies and would need to be requested from each company/facility individually. These records could not be obtained in the timeframe for the risk evaluation. This comment may be in reference to the National Emissions Inventory (NEI), which is compiled every 3 years for the purpose of supporting residual risk evaluations as required by Section 112 of the CAA. NEI contains air emission estimates, which sites estimate using a variety of methods, such as emission factors, mass balance, stack monitoring. Purchase and disposal records are not reported to NEI. However, NEI could not be used 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 methylene chloride. • The EFAST modeling program used in this assessment

	• One Committee member suggested the mass balance calculation be performed for each assessed facility, considering intake and documented disposal plus water and air releases. Another suggested releases from multiple facilities located in the same hydrologic unit be combined. • The Committee recommended that discharges estimated from the mass balance approach be used as input to a Fugacity level 3 or similar model to compare with (and supplement) any available environmental monitoring data.	does not offer the ability to model multiple releases within the same hydrologic unit or stream reach. While the majority of evaluated hydrologic units at the HUC8 level have a single releasing facility (73%), EPA recognizes this uncertainty and has added the following language to Section 4.4.1, "EPA did not consider releases' combined impact on concentrations in the same waterbody. This may lead to an underestimation of surface water concentrations in waterbodies with multiple releases coming from one facility or waterbodies with multiple facilities contributing releases."
Limitations of using TRI and DMR data to estimate releases		
SACC	**SACC COMMENTS:** • The lack of surface water monitoring data for MC was a concern, as was the insufficiency of just looking at TRI and DMR data for releases. Given that only facilities of a certain size are required to submit these reports, it is likely that overall release data are underestimated. • SACC members questioned why the quantitative environmental assessment is limited only to the measured water concentrations from the 2016 dataset and recommended that the discussion be expanded to better justify why all of the available data were not used. • The Committee expressed concern that monitoring data were obtained far away from the discharging facility.	• The environmental assessment was limited to 2016 to better harmonize with the estimated releases from the 2016 TRI and DMR releases. EPA's analysis uses TRI and DMR to estimate the highest local per site water releases of MC and is not intended to estimate overall releases. EPA's analysis uses TRI and DMR to estimate the highest local per site water releases of MC. A mass balance calculation for each assessed facility, considering intake and documented disposal plus water and air releases, is not useful for EPA's analysis, which is to estimate the highest local per site water releases of MC. • EPA used reasonably available data concerning monitored concentrations and reported releases of MC. The assumptions and uncertainties associated with using these data sources are discussed in Section 4.3. Included in those uncertainties is the distance and possible time of sampling in comparison to known releasers of MC.
62, 66, 73, 75	**PUBLIC COMMENTS:** • Using the TRI and DMR to estimate releases into the environment is not health-protective and	• EPA used the best available science and reasonably available data concerning known releases of MC. EPA's analysis uses TRI and DMR to estimate the highest local

	underestimates the true release of MC into the environment. • Reporting requirements limit the amount of entities providing information to the TRI. A facility is only required to report if it has ten or more full-time employees, is included in an applicable NAICS code, and manufactures, processes, or uses the chemical in quantities greater than a certain threshold. Companies producing, manufacturing, and using MC on a smaller scale are overlooked. • There are potential sources of emissions from sectors not covered by TRI reporting, such as oil and gas extraction. • For DMR, the EPA used the Water Pollutant Loading Tool within EPA's Enforcement and Compliance History Online to attain MC point source water discharge. States are only required to load "major" discharger data into DMR, at the discretion of the state. This is a massive uncertainty and flaw in the reporting system.	per site water releases of MC. The assumptions and uncertainties associated with using these data sources, such as limitations on required reporters, are discussed in Section 4.4.
Use of additional data sources for monitoring and release data		
SACC, 70, 73	**SACC AND PUBLIC COMMENTS:** • Consider exploring other potential data sources for monitoring and release data, such as the Association of Public Health Laboratories (APHL), the National Emission Standards for Hazardous Air Pollutants (NESHAP), and the Toxic Use Reduction Act (TURA). • Analytical data for soil, vapor, and water samples collected during subsurface or remediation investigations of regulated chemicals like MC are often required to be submitted in electronic data formats to state or regional regulatory agency; EPA should obtain and use these data.	• EPA did not find readily available information from APHL or TURA. • NESHAPs are air regulations that require companies to keep certain records; however, these records are retained by individual sites and companies and would need to be requested from each company/facility individually. These records could not be obtained in the timeframe for the risk evaluation. This comment may be in reference to the National Emissions Inventory (NEI), which 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

	• Some Committee members were concerned that EPA did not have adequate MC production use and discharge data and had to rely on industry data (e.g., from market reports). They were concerned that market reports and other industry data have not been evaluated for quality.	balance, stack monitoring. Purchase and disposal records are not reported to NEI. However, NEI could not be used 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 methylene chloride. • Industry data covers a wide range of data EPA reviewed in developing the COU and subsequent exposure scenarios included in the Risk Evaluation. Some data is self-reported by industry directly to EPA such as CDR and TRI. Both sources require a signed certification statement confirming that all information submitted on the form is complete and accurate to the best knowledge of the submitter. CDR and TRI also go through data quality processes to help reduce the issue of misreports. Other industry data have not been used directly for the water release assessment for MC. EPA also consults trade publications and technical references that go through a vetting and review process prior to publication. Information also is collected through direct communication with industry, trade associations, or other stakeholders (including our federal partners). The information collected from these sources is helpful in refining EPA's understanding of the information submitted by industry through CDR and TRI and often provides much needed context to those data.
Model inputs and assumptions		
SACC	**SACC COMMENTS:** • Better document the uncertainty of model inputs and assumptions and perform sensitivity analysis to categorize the impact of this uncertainty on exposure estimates. For example, the removal from wastewater treatment was estimated to be	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

	57% and this value was used in the model with no variation or uncertainty considered.	in the STPWIN model are reported in high-quality data sources and align with expected values for MC, and thus are of high-confidence. The uncertainty in biodegradation rates is discussed in Section 2.1.3, and MC removal from wastewater by biodegradation was assessed to range from negligible to complete depending on the conditions in a given WWTP. The MC 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 (57%) aligns with the measured overall removal reported by TRI (54%).
68	**PUBLIC COMMENTS:** • EPA noted that due to its high Henry's law constant and vapor pressure, MC is expected to volatilize rapidly from wastewater (p. 64). However, it did not consistently or appropriately apply this aspect to its exposure estimations. For example, a number of the active releasers identified in Table Apx E-4 (pp. 572-591) are indirect releasing facilities, meaning that their wastewater is piped and sent to another treatment facility, typically a POTW. The EPA analysis does not consider dissipation in the sewers prior to wastewater treatment, also referred to as "pipeloss" (Matthjis et al., 1995). In addition, EPA estimated that the half-life of MC in a model river will be 1.1 hours (p. 64); however, it did not appear to apply that half-life when considering effluent discharges to a receiving stream and the impact on downstream concentrations. • EPA stated that, "[t]wenty days of release was modeled as the low-end release frequency at which possible ecological chronic risk could be determined (pp. 79-80)." o The 20-day release assumption should be better justified. While it may seek to replicate a	• As other comments have pointed out, Henry's law constants and vapor pressures indicate partitioning directions but not rates. Thus, the risk evaluation has been edited and no longer states that MC will volatilize "rapidly." • Pipe loss was not considered in our estimated releases due to lack of information about the rates that would occur for a chemical such as MC or the distances between transferring facilities to indirect dischargers. • EPA added more explanation about the 20-day release assumption to Section 2.3.1.2.1 E-FAST Calculations in the Risk Evaluation. The 20-day chronic risk criterion is derived from partial life cycle tests (e.g., daphnid chronic and fish early life stage tests) that typically range from 21 to 28 days in duration. Additionally, EPA included additional analysis of surface water concentrations, for the 5 facilities that showed risk in the environmental risk characterization section. The analysis now includes modeling of all facilities with known releases of MC to surface water according to TRI and DMR data. Any facilities with risk then go through an additional analysis with surface water concentrations estimated using

	worst-case situation, there is no basis in fact that any particular facilities discharge their effluents accordingly. o The 20-day release scenario is coupled with 7Q10 dilution. The odds of the 20 days falling within the 7Q10 window are small and overly conservative. EPA should assume mean flow if it is going to apply an arbitrary, conservative, limited release scenario. o If this arbitrary assumption results in exceedance of the COC, EPA should not conclude that the situation constitutes an unreasonable risk but that additional analysis at a higher tier would be justified.	fugacity models in EPI Suite™, which take volatilization into account, and information from EXAMS. The results show that environmental conditions can produce a wide range of surface water concentrations which encompasses concentrations estimated in E-FAST. • The use of the 7Q10 flow value is intended to represent a protective evaluation of low flow conditions where environmental and human populations may be most affected. The predicted concentrations associated with different flow metrics are available in supplementary materials, but the modeling with EFAST does not allow for evaluation of days of exceedance outside use of the 7Q10 flow metric.
73	**PUBLIC COMMENTS:** • EPA found that releases from certain disposal and recycling facilities would result in surface water concentrations well above the COC for MC (pp. 427-28). But EPA's analysis may still have underestimated the total risk from these releases. For example, when estimating the releases from one facility where the surface water concentration exceeded the COC, EPA "assumed 57% removal of methylene chloride before it was released to surface water" (p. 288). EPA did not establish that this assumed removal actually occurs, so EPA may be underestimating the total risk presented by releases from this facility. • Releases were not considered together and combined when appropriate. For example, three of the facilities where modeled surface water concentrations exceed the chronic COC engaged in transfers to the same facility – Clean Harbors Baltimore (p. 287). Particularly given that the modeled results for each of the three facilities	• The EPI Suite™ model that estimates removal during wastewater treatment (STPWIN) estimated that 57% of MC in influent water will be removed via abiotic processes (sorption to sludge and volatilization to air) in a conventional wastewater treatment plant (WWTP) with secondary treatment via activated sludge. This does not include possible biodegradation, but because there is a range of reported aerobic biodegradation rates EPA assessed that removal via biodegradation may range from negligible to complete depending on factors such as the microbial consortium in a given WWTP, its pre-adaptation to MC, and biomass concentration in the activated sludge stage. Discussion of this uncertainty has been added to Section 2.1.3. Thus, 57% removal was expected to be the more protective value to use. The estimated 57% removal aligns with the WWTP removal efficiency for MC reported by TRI (54%), which was used in exposure calculations. • As mentioned, EPA did not consider releases' combined

	indicate a risk when analyzed separately, EPA should have considered how they may combine to present an even greater risk.	impact on concentrations in the same waterbody. EPA added language to the Key Assumptions and Uncertainties Section describing how this may lead to an underestimation of surface water concentrations in waterbodies with multiple releases coming from one facility or waterbodies with multiple facilities contributing releases.
Climate change impact on stream flow rates		
49, 75	**PUBLIC COMMENTS:** • Climate change is likely to affect stream flow rates (EPA used 15-30-year-old stream flow data to calculate surface water concentrations for MC), contaminant fate and transport, human sensitivity to chemical stressors, and even the use of personal protective equipment (PPE) (which can be even more burdensome in higher temperature). To the extent that specific impacts are difficult to predict, EPA should account for that uncertainty through sensitivity analyses, a broader range of temperature-related assumptions, or additional UFs.	As mentioned, climate change is anticipated to affect a variety of factors considered in this assessment. The stream flow data used represents the most comprehensive and accurate nationwide datasets available for evaluation and analysis. The assumptions and uncertainties of this dataset are discussed in full within Section 4.3. EPA did not find reasonably available information on impacts of climate change on use of PPE, and EPA does not have methods to conduct such sensitivity analyses on use of PPE. 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. Rather, these risk estimates are part of EPA's approach for developing exposure assessments for workers that use the reasonably available information to construct exposure scenarios that are anchored in the real-world use of chemicals. 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., 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), 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 MC, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE. Generally, the predicted increases in atmospheric temperatures will not modify physical-chemical or fate properties sufficiently to impact the environmental fate and transport assessment. Based on its vapor pressure (435 mmHg at 25°C) MC is expected to volatilize from dry surfaces. Increasing temperatures from standard test conditions at 25°C to 30°C would increase vapor pressure by approximately 20%, which would generally increase MC volatilization and shift MC from soil and other dry media compartments to the air. Water solubility would increase, but MC is soluble in water (13 g/L at 25°C). MC's enthalpy of solvation, needed to correct its air-water partition coefficient for an increase in temperature, is not readily available; thus, EPA cannot at this time assess how increasing temperatures will change air-water partitioning and whether it will increase volatilization from water to air.
No requirement that release be tied to conditions of use		
73	**PUBLIC COMMENTS:** • Under TSCA, EPA must conduct risk evaluations that consider all "reasonably available" information relating to a chemical substance,	EPA has considered releases that are not attributable to specific conditions of use, and these releases are addressed in Section 2.2.2.22.

	including information that may not be tied to a specific condition of use, 15 USC § 2625(k). There is no basis in TSCA for EPA to ignore environmental releases of a chemical simply because it has not determined or cannot determine how much of the exposure is attributable to a particular condition of use.	
Consider disposal and spill related releases		
66, 49, 75	**PUBLIC COMMENTS:** • The draft MC risk evaluation does not evaluate the risks associated with disposal-related releases, including reasonably foreseen spills and leaks during production, use, distribution, and disposal. In its report on the 1,4-dioxane and HBCD risk evaluations, the SACC noted EPA's failure to consider releases associated with disposal, including "the movement and breakdown of disposed materials from soils and in particular from landfills into air and waterways" and recommended that "EPA should also include a spill scenario as potential and probable occurrences in the occupational environment." Since then, the Ninth Circuit has affirmed that "TSCA's "definition of 'conditions of use' clearly includes uses and future disposals of chemicals," as well as "spills, leaks, and other uncontrolled discharges" emanating from landfills, Superfund sites, and other disposal locations. • Household disposal is neglected. It is not reasonable to assume all containers on the consumer end are treated properly. There will be a significant amount of aerosol containers end up in landfills or other places. Thus, it will increase the amount of MC in the soil or water.	Spills and leaks generally are not included within the scope of a TSCA risk evaluation. EPA is exercising its authority under TSCA to tailor the scope of the risk evaluation for MC, rather than evaluating activities which are determined not to be circumstances under which MC is intended, known or reasonably foreseen to be manufactured, processed, distributed, used, or disposed of, or environmental exposure pathways addressed by another EPA-administered statute and associated regulatory program. First, EPA does not identify MC spills or leaks as "conditions of use." EPA does not consider MC spills or leaks to constitute circumstances under which MC 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 MC 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 MC could be considered part of the listed lifecycle stages of MC, EPA has "determined" that spills and leaks are not circumstances under which MC 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 to exclude MC spills and leaks from the scope of the MC 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, 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 MC 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 MC 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 MC to be COUs. Second, even if MC 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, exclude certain activities that EPA has determined to be conditions of use 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...." The approach discussed in the Risk Evaluation Rule and applied in the problem formulation documents 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). Following coordination with EPA's Office of Land and Emergency Management (OLEM), EPA has found that exposures of methylene chloride 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 methylene chloride as hazardous waste no. U080). As a result, EPA believes it is both reasonable and prudent to tailor the TSCA risk evaluation for methylene chloride 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. Finally, EPA notes that the Ninth Circuit in *Safer Chemicals Healthy Families v. EPA* presented examples of circumstances that may qualify as disposal but did not establish a "precise meaning of 'disposal.'" 943 F.3d 397, 426 (9th Cir. 2019). The Court also did not opine on EPA's authority to determine the circumstances under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used or disposed of. 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."
Coordination with other statutes		
SACC	**SACC COMMENTS:** • Several Committee members expressed concern that large quantities of MC are volatilized to ambient air from diverse and disperse uses and that there is no condition of use that provides a basis for setting any limit on these emissions. While EPA asserts that the CAA can be used to control these emissions, Committee members thought the CAA would address only a fraction of total emissions, i.e., only from Major Sources as defined by the 1990 CAA Amendments.	Emissions to ambient air from commercial or industrial stationary sources, or inhalation exposures of terrestrial species are under the jurisdiction of the Clean Air Act (CAA). Additionally, based on its vapor density (2.93 relative to air) and persistence in the atmosphere (photolysis half-life by OH• reaction = 79 days), MC vapor may accumulate under specific conditions, but typically will disperse readily into the air.
75, 77, 73, 33 (3)	**PUBLIC COMMENTS:** • EPA's exclusion of all environmental releases violates TSCA and disregards additional human	• Clarifying language about what pathways are addressed under other statutes has been added to Section 1.4.2 of the Risk Evaluation.

	exposure pathways that contribute to aggregate exposure and risk. This approach is an unlawful interpretation of TSCA, has twice been rejected by SACC and overlooks the widespread presence of MC in environmental media to which millions of people are exposed. Congress designed TSCA to fill "regulatory gaps" through a comprehensive approach to chemical risk management that considered "the full extent of human or environmental exposure," H.R. Rep. No. 94-1341. TSCA's role in assessing these aggregate risk and exposure pathways is unique and not duplicated in other statutes and must be reflected in the MC risk evaluation. The legislative history of the original law confirms that Congress recognized that then-existing environmental laws were "clearly inadequate" to address the "serious risks of harm" to public health from toxic chemicals. While other federal environmental laws focused on specific media, such as air or water, none gave EPA authority to "look comprehensively" at the hazards of a chemical "in total." S. Rep. No. 94-698. • Despite recognizing MC's high volatility, high vapor density, and long-range transport in air (p. 64) – all factors that increase potential air exposures to terrestrial organisms – EPA ignored inhalation exposures to terrestrial species, stating: "stationary source releases of MC to ambient air are adequately assessed and any risks effectively managed under the jurisdiction of the Clean Air Act (CAA)" (p. 299). This exclusion is illegal. MC's status as a CAA HAP does not justify ignoring air emissions in the draft evaluation. Title III of the CAA initially mandates technology-based – not risk-based – emission limits. Once these limits are in place, the law gives EPA at least	• The purpose of risk evaluation under TSCA is to determine whether a chemical substance presents an unreasonable risk to health or the environment, under a TSCA 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 managed under the jurisdiction of the Clean Air Act (CAA). • Based on the Guidance for Ecological Soil Screening Levels (EPA, 2003a, b) document, for 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).

	eight more years to evaluate residual risks and potentially set risk-based emission standards under CAA Section 112(f). However, these standards only consider emission-related risks, and thus do not take into account aggregate health risks from all sources of exposure. Moreover, the CAA mandates emission standards for "major" sources, which are defined as facilities that emit more than 10 tons per year of any single HAP or 25 tons per year of all HAPs. This definition would not cover the thousands of smaller establishments that in the aggregate account for substantial MC air emissions. These facilities may be regulated as "area sources" under the CAA but would not be subject to mandatory, chemical-specific, risk-based standards.	
68	**PUBLIC COMMENTS:** • EPA OPPT's decision to "scope in" the ambient water pathway and to conduct an aquatic life risk evaluation in the MC draft TSCA risk evaluation raises serious questions about the overlapping jurisdiction of TSCA and other environmental laws, the TSCA Section 9 coordination requirements, and EPA's ability to efficiently conduct risk evaluations in the longer term.	Communication and coordination between program offices within EPA occur regularly on TSCA-related efforts. While EPA has recommended water quality criteria for protection of human health for MC (EPA-HQ-OW-2014-0135), it has not developed CWA section 304(a) recommended water quality criteria for the protection of aquatic life for MC. As a result, the ambient water pathway underwent aquatic life risk evaluation under TSCA. Additionally, clarifying language about what pathways are addressed under other statutes has been added to Section 1.4.2 of the Risk Evaluation.

Environmental Hazard		
EPA evaluated environmental hazards for aquatic species from acute and chronic exposure scenarios. **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?		
#	**Summary of Peer Review Comments for Specific Issues Related to Charge Question 3**	**EPA/OPPT Response**

Key study not publicly available, lack of adequate data		
49	**PUBLIC COMMENTS:** • TSCA expressly prohibits EPA from withholding health and safety studies, including studies of a chemical's ecological toxicity, but EPA has not provided public access to all studies it relied on for its environmental risk evaluations (e.g., 1987 study by E I Dupont de Nemours & Co. Flow-Through Acute 96-Hour LC50 of Methylene Chloride to Rainbow Trout, has not been made available online). All of the cited references in the risk evaluation should be made available for public review.	The EI Dupont de Nemours & Co study is publicly available with the HERO ID of #4213817. All cited references are available for public review.
49, 75	**PUBLIC COMMENTS:** • EPA lacks adequate data to evaluate ecological risk. EPA does not have any studies of MC's effects on terrestrial or sediment-dwelling species (p. 299). EPA also has no "chronic studies that encompassed amphibian metamorphoses and adult reproductive stages of the amphibian life-cycle" (p. 204) and "no acceptable chronic exposure aquatic invertebrate studies" (p. 205). Without these data, EPA cannot fully evaluate MC's environmental risks.	EPA believes it has adequate hazard data to evaluate the environmental risks of MC to aquatic organisms. MC is not expected to bioaccumulate in tissues, and concentrations will not increase from prey to predator in either aquatic or terrestrial food webs. Based on the Guidance for Ecological Soil Screening Levels (EPA, 2003a, b) document, for 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 characterized terrestrial organism exposures to MC as "not of concern" based on estimates of soil concentrations several orders of magnitude below concentrations observed to cause effects in terrestrial organisms during Problem Formulation. Therefore, EPA had adequate information to conclude that terrestrial species would not be a concern. EPA has added language to the final risk evaluation document in Section 4.1.4 explaining this rationale. EPA used the reasonably available data to assess sediment invertebrates. Because MC is not expected to sorb to sediment and will instead remain in pore water,

		daphnia which feed through the entire water column were deemed to be an acceptable surrogate species for sediment invertebrates consistent with EPA/OPP guidance, which lists several considerations for determining the likelihood of exposure and toxicological relevance of exposure to sediment-dwelling organisms (https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/toxicity-testing-and-ecological-risk-assessment). Therefore, EPA did not view this as a data need. Additionally, Staples et al. (1985) stated that the median concentration measured in sediment was 13 µg/kg, equivalent to 13 ppb, which is more than 2 orders of magnitude below the chronic (1,800 ppb) and acute COC (36,000 ppb) values estimated for sediment invertebrates by read-across from COCs reported for aquatic invertebrates.
Selection of point of departure (POD) for acute environmental hazard		
SACC	**SACC COMMENTS:** • The Committee considered the LC50 endpoint not protective of environmental receptors and argued that it is incorrect to use the geometric mean of LC50 values from multiple species as the measure of lethality. The committee recommended instead that EPA develop LC01 values for different species where possible and select the lowest value as the POD. In that light, the Committee considered the LC01 of 9.7 µg/L for the common European frog (*Rana temporaria*) to be a more easily justified POD than the LC50 for Northern salamander *(Ambystoma gracile*) of 23.03 mg/L, while noting that the LC50 of 23.03 mg/L for *A. gracile* would still be more appropriate than the value proposed in the current risk evaluation, because this lowest measured LC50	• In accordance with EPA guidance, LC50s are commonly used as a measure of acute hazard to aquatic organisms (EPA, 2013, 2012b). After considering this comment, EPA determined that no change is needed. LC01 values were only reasonably available for *R. catesbeiana* (0.09 mg/L) and *R. temporaria* (0.07 mg/L), which were the most sensitive species tested. Toxicity data for other amphibian and fish species was not sufficient to calculate LC01s, and/or LC10s. EPA added LC01 values for the two *Rana* species to the hazard table and summary, but used the geometric mean of the LC10s (0.9 mg/L from LC10s of 0.98 mg/L and 0.82 mg/L, respectively) as the lowest value for the concentration of concern because, as both Birge, et al. (1980) and Black et al., (1982) noted, it is more

	represents 17% of amphibian species in a species sensitivity distribution. • The Committee further recommended that if calculation of LC01 values is not considered a viable approach, then an assessment factor of 100 (see Kienzler et al., 2017) should be applied to the daphnia toxicity estimate proposed in the current risk evaluation.	likely to have substantial reproductive impairment resulting in population-level effects. • 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. EPA will consider the Kienzler et al., 2017 study in its assessment. Until the body of scientific evidence for assessment factors is evaluated, EPA will continue to use OPPT methodology as cited in the risk evaluation (EPA, 2013, 2012b) 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 MC, which produce toxicity from simple narcosis.
49, 75, 73	**PUBLIC COMMENTS:** • EPA's toxicity assessment methodology for MC leaves the most sensitive species at risk. EPA does not select COCs based on the most sensitive species and the most sensitive endpoint, as it has done in other risk evaluations. Instead, EPA averages data across studies of different species and different endpoints and sets the COC based on their geometric mean (e.g., for acute toxicity in freshwater fish, EPA used LC50 = 242.41 mg/L, calculated as geometric mean of available studies, rather than LC50 = 108 mg/L, based on the most sensitive species, rainbow trout).	EPA used reasonably available data for estimating lethality and overall effects to aquatic organisms. EPA used a geometric mean using toxicity values from more than one species of amphibian, because the toxicity values were very close to one another, and taking more than one toxicity value into consideration from more than one species gave EPA higher confidence in the value that EPA used to calculate its COC. To account for species that may be more sensitive that are not included in the COC calculation EPA used an assessment factor (AF) of 10, consistent with OPPT methodology cited in the risk evaluation (EPA, 2013, 2012b) This AF is higher than the AF of 5 normally used to calculate acute COCs for aquatic invertebrates and fish, because EPA wanted to incorporate the added uncertainty around amphibians into the COC.

MC RESPONSE TO COMMENT

49, 75	**PUBLIC COMMENTS:** • The commenters disagreed with EPA's assessment of toxicity in algae. EPA selected a COC of 33.09 mg/L, based on a study of *C. reinhardtii*, even though, in another study that EPA assigned an overall quality level of medium, MC killed *V. steinii*, a different algal species, at a much lower concentration, 0.002 mg/L (p. 206). EPA stated that "[t]he study supports the need for assessment factors to establish the hazard values to account for more sensitive species," but the 10-fold "assessment factor" applied by EPA is not nearly large enough to account for the more than 10,000-fold difference in results between the studies.	The 2003 study by Ando, et al. (2003) referred to by the commenter used an indirect measurement of algal cell growth, chlorophyll *a*, that is not relevant for hazard evaluation. The study also did not have critical details, such as analytical measurement of test concentrations, chemical substance source or purity, or an EC50 calculated from the relative absorbance results, so EPA used this value qualitatively in the risk evaluation. EPA added clarifying language to the risk evaluation to address this issue.
SACC	**SACC COMMENTS:** • Evaluation of the aquatic invertebrate toxicity data showed that the geometric mean for aquatic invertebrates (i.e., 179.98 mg/L; p. 207) or the underlying values for aquatic invertebrate toxicity (p. 204) seem to be in error.	The geometric mean for aquatic invertebrates included definitive values only.
Use of Daphnia as a surrogate species for estimating hazard in sediment invertebrates		

SACC, 73	**SACC AND PUBLIC COMMENTS:**
	• Daphnia was used as a surrogate species for estimating hazard in sediment invertebrates (p. 205).
	  ○ Since daphnia feed through the entire water column and in sediment, it is improper to consider daphnia as representative of sediment-dwelling organisms.
	  ○ If daphnia *must* be used, then the assessment factor or UF should be higher, as noted by Keinzler et al. (2017).
	  ○ EPA should have identified this as a data gap and taken steps to address it using its information authorities under TSCA.
		EPA used the reasonably available data to assess sediment invertebrates. Because MC is not expected to sorb to sediment and will instead remain in pore water, daphnia which feed through the entire water column were deemed to be an acceptable surrogate species for sediment invertebrates. Therefore, EPA did not view this as a data need.
		
		Additionally, Staples et al. (1985) stated that the median concentration measured in sediment was 13 µg/kg, equivalent to 13 ppb, which is more than 2 orders of magnitude below the chronic (1,800 ppb) and acute COC (36,000 ppb) values estimated for sediment invertebrates by read-across from COCs reported for aquatic invertebrates.

Chronic toxicity to aquatic invertebrates		

73	**PUBLIC COMMENTS:**
	• EPA states "there were no acceptable chronic exposure aquatic invertebrate studies, so EPA applied the acute-to-chronic ratio (ACR) of 10… to estimate the freshwater aquatic invertebrate chronic exposure toxicity value" (p. 205).
	  ○ EPA provided no justification for its application of an 'acute-to-chronic ratio' or its specific value of 10. A search of the literature indicated that an ACR of at least 100 may be needed to be sufficiently protective.
	  ○ EPA should have identified this as a data gap and taken steps to address it using its information authorities under TSCA.
		In the absence of chronic aquatic invertebrate data, EPA applied an ACR of 10 to the acute aquatic invertebrate data to estimate a chronic toxicity value according to current EPA methods under TSCA (EPA, 2013, 2012b). EPA decided to do this, because aquatic invertebrates were not the most sensitive taxa represented in the acute data. Therefore, EPA did not view this as a data need.

Selection of POD for chronic hazard to amphibians		
SACC, 73	**SACC AND PUBLIC COMMENTS:** • A 9-day exposure (p. 212) is not a chronic exposure for salamander. • These durations fall far short of the recommended length of amphibian assays according to OECD test guidelines and accepted practice. The Amphibian Metamorphosis Assay (OECD 231) calls for an exposure duration of 21 days, whereas the Larval Amphibian Growth and Development Assay guideline (OECD 241) requires the assessment be run for 16-17 weeks. • An additional AF of 10 should be applied with the existing AF of 10 to produce a value of 0.09 mg/L that would seem to be consistent with the conclusions of the authors (Black et al., 1982). • Calculating an acute-to-chronic estimate using the Acute-to-Chronic (ACE) tool could provide corroborative evidence in support of this value. • A benchmark dose lower bound (BMDL) could be estimated using the Black et al. (1982) data.	• In the absence of chronic amphibian studies, EPA viewed the amphibian study 4-days post-hatch (8-9 days total) as sub-chronic and applied an AF of 10 to derive a chronic hazard value per current OPPT methodology (EPA, 2013, 2012b). • EPA is in the process of evaluating the body of reasonably available literature on AF 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 but will use current OPPT methodology for the first 10 priority chemicals, including MC. Neutral organic substances such as MC produce toxicity from simple narcosis. EPA applies an AF of 10 to chronic toxicity values to derive chronic hazard values for aquatic organisms exposed to this class of chemicals under current OPPT methodology (EPA, 2013, 2012b). EPA feels confident that the AF of 10 applied to the sub-chronic toxicity value for amphibians is adequately protective of these species. The amphibian chronic

		hazard value of 0.9 mg/L is similar to but more protective than the fish chronic hazard value of 1.5 mg/L and more protective than the amphibian chronic value of 2.6 mg/L (derived by applying the ACR of 10 to the geometric mean of amphibian acute hazard values). • EPA will consider the ACE tool in its effort to evaluate the body of available literature on AF (including ACR ratios) in the future, but used current OPPT methodology for the first 10 priority chemicals, including MC. EPA examined whether benchmark dose modeling could be applied to the toxicity data from Birge, et al. (1980) and Black et al., (1982) used to derive the acute and chronic Concentrations of Concern using the peer-reviewed Benchmark Dose Software (BMDS) (https://www.epa.gov/bmds/about-benchmark-dose-software-bmds). Benchmark dose modeling is the preferred method used in human health fields to predicting toxicity effect values for a given endpoint and study. Its utility translates to ecotoxicity studies, where its use in generating LCx or ECx values can help to remove biases due to experimental design (*i.e.* what concentrations are chosen), allow for the inclusion of all toxicity data points, and allow for model fitting specific to the shape of different dose-response curves, as compared to traditional LOEC/NOEC methodologies. EPA found that benchmark dose modeling was not possible with the data provided in Birge, et al. (1980) and Black et al., (1982). This is because it was not possible to back-calculate a measure of error (STD/STE) for either paper because the experiments utilized one tank replicate

		per concentration, and the BMDS requires a measure of error for model calculation. However, EPA has high confidence in the toxicity values provided by both papers because the study authors did apply an appropriate modeling technique (log-probit analysis) to generate their LC10 and LC50 estimates for fish and amphibian species.
Selection of POD for chronic hazard to fish		
SACC	**SACC COMMENTS:** • The Committee did not agree with the selection of 5.55 mg/L as the no-observed-effect concentration (NOEC) for teratic larvae in the rainbow trout study (p. 207) since teratogenic effects were observed at this value. • Black et al. (1982) corrected survival numbers for control survivals (p. 205). Therefore, the 85% survival was relative to control survival. Thus, there is no rationale for excluding low concentration effects. A NOEC cannot reasonably be defined as a concentration, 0.41 mg/L, in which 15% mortality occurred. • There was a lower concentration of 0.042 mg/L, which demonstrated a 93% survival. The value of 0.041 mg/L would be the more appropriate NOEC for this study. • Immobile fish (p. 203) in this study could be considered mortalities in current testing protocols. The Agency should justify not considering immobile fish as mortalities.	• The authors did not establish a NOEC, LOEC, or LC10 for fish for MC as they did for other substances in the study. As a result, these values were not extracted during data extraction (only LC50s were established by the authors for MC). • EPA agrees that the percent larval survival at 0.042 mg/L (92%) and 0.41 mg/L (85%) suggest (by calculating with geometric mean) a LC10 falling around 0.13 mg/L. However, in the absence of a NOEC/LOEC for MC by the authors and resulting uncertainty in the statistical significance of the values, EPA established the NOEC as 0.41 mg/L and the LOEC as 5.55 mg/L (the next highest concentration) in order to not be over-conservative. The geometric mean fish ChV of 1.51 mg/L is also in line with the amphibian ChV of 0.9 mg/L, therefore EPA has greater confidence in this value for the fish ChV. • EPA determined that fish immobilization may be a temporary narcosis from which fish may recover after exposures. Although predation may occur as a result of immobilization, it is not necessarily mortality.
A hazard assessment for terrestrial organisms is needed		

MC RESPONSE TO COMMENT

SACC, 73	**SACC AND PUBLIC COMMENTS:** • The Committee disagreed with the characterization of environmental hazard in the risk evaluation and recommended addition of an assessment of potential exposures to terrestrial vertebrates through inhalation and soil contact, pathways that were dismissed without sufficient justification in the risk evaluation.	MC is not expected to bioaccumulate in tissues, and concentrations will not increase from prey to predator in either aquatic or terrestrial food webs. Based on the Guidance for Ecological Soil Screening Levels (EPA, 2003a, b) document, for 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 characterized terrestrial organism exposures to MC as "not of concern" based on estimates of soil concentrations several orders of magnitude below concentrations observed to cause effects in terrestrial organisms during Problem Formulation. EPA has added language to the final risk evaluation document in Section 4.1.4 explaining this rationale.
The assessment needs to consider threatened and endangered species, especially amphibians		
SACC	**SACC COMMENTS:** • The Committee recommended that the risk evaluation include an analysis of how home ranges of threatened and endangered species, including amphibians, overlap with known source areas impacted by MC releases, e.g. by use of U.S. Geological Survey (USGS) maps (Zogorski et al., 2006) and overlays of species ranges from E-FAST.	• The TSCA risk evaluation focuses on exposures to particular species and environmental receptors, and appropriately considered impacts to affected species.
Environmental hazard – general comments		
SACC	**SACC COMMENTS:** • The risk evaluation citation "Wilson, JEH. (1988)" is incomplete. It does not contain the name of the journal or the book. • Even though the purity of the test substance was not specified in this paper, the Committee questioned whether the purity could be assigned or assumed using the average purity of MC on the market.	• The full citation (Wilson, 1998) was updated in HERO read: Wilson, J.E.H., "Developmental Arrest in Grass Shrimp Embryos Exposed to Selected Toxicants," *Environmental Toxicology and Risk Assessment: Seventh Volume, ASTM STP 1333*, E.E. Little, A.J. DeLonay, and B.M. Greenberg, Eds., American Society for Testing and Materials, 1998.

		• EPA considered converting the Wilson study using a range of purity assumptions but determined that these would add to the uncertainty for the test results. Therefore, the paper was used qualitatively.
SACC	**SACC COMMENTS:** • The summary of environmental hazard in Section 3.1.5 needs one or two concluding sentences that compare effects of MC across different trophic levels.	• Concluding sentence added.
SACC	**SACC COMMENTS:** • The EC50 values of 242.41 and 135.81 mg/L (p. 203) cannot be known to this level of precision.	• Rounding to 3 significant figures where possible in the risk evaluation.
SACC	**SACC COMMENTS:** • The species and LC50 values for each study used should be listed along with an indication of whether measured or nominal data were used. • Many of these LC50 values are from studies that do not report any measured or nominal concentrations for exposures.	• Species and whether studies report nominal or measured concentrations are included in the hazard summaries and in the Systematic Review Supplemental File: Data Quality Evaluation of Environmental Hazard Studies. • All LC50 values were from studies that reported these values, as indicated in the hazard summaries.
SACC	**SACC COMMENTS:** • The Committee concurred that amphibians are likely among the most sensitive aquatic species for MC (Risk Evaluation, pp. 29, 285). • This conclusion suggests that obtaining toxicity data on amphibians and/or accounting for amphibian sensitivity should be a part of all TSCA risk evaluations. • Manufacturers and users of chemicals considered for regulation under TSCA should be required to provide data on amphibian toxicity.	EPA considered amphibian data by using amphibian toxicity data to calculate the concentration of concern. Variation in species sensitivity was accounted for by using an assessment factor of 10. EPA considers reasonably available data on a chemical by chemical basis and would exercise any necessary information gathering in a fit-for-purpose manner, as was the case for PV29. As part of the consideration of reasonably available information, EPA considers data gaps and the need for additional information as appropriate.

MC RESPONSE TO COMMENT

Occupational and Consumer Exposure
EPA evaluated acute and chronic exposures to workers for conditions of use in industrial and commercial settings. For exposure via the inhalation pathway, EPA quantified occupational exposures for both workers and occupational non-users based on a combination of monitoring data and modeled exposure concentrations. For exposure via the dermal route, EPA modeled exposure for workers, accounting for the effect of volatilization. EPA assumed dermal contact with liquids would not occur for occupational non-users. EPA assumed that workers and occupational non-users would be adults of both sexes (>16 and older, including women of reproductive age). **Charge Question 4.1.** Please comment on the approaches and estimation methods, models, and data used in the occupational exposure assessment. **Charge Question 4.2.** Please provide any specific suggestions or recommendations for alternative data or estimation methods that could be considered by the Agency for conducting the occupational exposure assessment. **Charge Question 4.3.** EPA assumed the following default surface area value for modeling dermal exposures for occupational exposure scenarios for which surface area data were not available: a high-end value of 1070 cm^2, which represents two full hands (mean value for males) in contact with a liquid. Please provide input on data sources and specific alternative values relevant to the uses. To estimate ONU inhalation exposure, EPA reviewed personal monitoring data, area monitoring data and modeled far-field exposure concentrations. When EPA did not identify personal or area data on or parameters for modeling potential ONU inhalation exposures, EPA assumed ONU inhalation exposures could be lower than worker inhalation exposures however relative exposure of ONUs to workers could not be quantified. When exposures to ONUs were not quantified, EPA considered the central tendency from worker personal breathing zones to estimate ONU exposures. **Charge Question 4.4.** Please comment on the assumptions and uncertainties of this approach. **Charge Question 4.5.** Are there other approaches or methods for assessing ONU exposure for the specific condition of use? Consumer exposure estimates were developed for the conditions of use for inhalation and dermal exposures to consumers. EPA did systematic review, collected data from available sources and conducted modeling for estimating consumer inhalation and dermal exposures using the CEM model. Product specific consumer monitoring information was not identified during the systematic review process, therefore, model inputs related to consumer use patterns (duration of use, mass of product used, room of use, and similar inputs) are based on survey data found in the literature as described and referenced within the methylene chloride draft risk evaluation. Weight fraction of chemical within products are based on product specific safety data sheets (SDS). Default values utilized within the models are based on literature reviewed as part of model development as well as EPA's Exposure Factors Handbook. **Charge Question 4.6.** Please comment on the approaches, models, exposure or use information and overall characterization of consumer inhalation exposure for users and bystanders for each of the identified conditions of use. What other additional information, if any, should be considered? **Charge Question 4.7.** Please comment on the approaches, models, exposure or use information and overall characterization of consumer dermal exposure for each of the identified conditions of use. What other additional information or modeling approaches, if any, should be considered?

Charge Question 4.8. Dermal exposure was evaluated using the absorption method submodel within CEM. 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.

#	Summary of Peer Review Comments for Specific Issues Related to Charge Question 4	EPA/OPPT Response
Conditions of use		
49, 72, 73, 75, 76, SACC	**SACC COMMENTS:** • Several conditions of use described under both consumer and "industrial and commercial" were not evaluated under consumer uses. Ensure that these conditions of use do not exist in the consumer space and evaluate the condition of use if they are reasonably foreseen to exist. **PUBLIC COMMENTS:** • EPA excluded consumer uses such as metal products not covered elsewhere, apparel and footwear care products, and laundry and dishwashing products from its analysis of consumer uses; EPA included these conditions of use as industrial and commercial uses. • Given MC's industrial and commercial uses, the potential for these uses to be expanded to consumer use is reasonably foreseeable. • EPA also excluded reasonably foreseen conditions of use in the workplace including exposure from spills and leaks, "take-home exposures", exposures to maintenance staff, and exposure to workers	• EPA's risk evaluation addresses consumer uses. EPA has determined that there is no known, intended, or reasonably foreseen consumer use of certain conditions of use, including metal products not covered elsewhere, apparel and footwear care products, and laundry and dishwashing products. There are only industrial and commercial uses of methylene chloride for these conditions of use, and these conditions of use were assessed. • EPA included ONUs who are defined in section 2.4.1 as "working in the general vicinity of workers but do not handle chemical substances and do not have direct dermal contact with chemicals being handled by the workers." Maintenance staff are a subset of ONUs and as such are not excluded from the risk evaluation. Also, workers at small facilities are not excluded, and the PPE use expectation is applicable to all facilities (OSHA regulations cover small facilities). • 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. Spills/leaks • Spills and leaks generally are not included within the scope of a TSCA risk evaluation. EPA is exercising its authority under TSCA

	at small facilities where routine PPE use is less likely to be valid. • EPA should clarify its treatment of these conditions of use.	to tailor the scope of the risk evaluation for MC, rather than evaluating activities which are determined not to be circumstances under which MC is intended, known or reasonably foreseen to be manufactured, processed, distributed, used, or disposed of, or environmental exposure pathways addressed by another EPA-administered statute and associated regulatory program. • First, EPA does not identify MC spills or leaks as "conditions of use." EPA does not consider MC spills or leaks to constitute circumstances under which MC 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 MC 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 MC could be considered part of the listed lifecycle stages of MC, EPA has "determined" that spills and leaks are not circumstances under which MC 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 to exclude MC spills and leaks from the scope of the MC risk evaluation. The exercise of that authority is informed by EPA's expertise 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 expertise 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, 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 MC 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 MC 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 MC to be COUs. • Second, even if MC 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, exclude certain activities that EPA has determined to be conditions of use 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...." The approach discussed in the Risk Evaluation Rule and applied in the problem formulation documents 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). • Following coordination with EPA's Office of Land and Emergency Management (OLEM), EPA has found that exposures of methylene chloride 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 methylene chloride as hazardous waste no. U080). As a result, EPA believes it is both reasonable and prudent to tailor the TSCA risk evaluation for methylene chloride 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.
45	**PUBLIC COMMENTS:** • Some of the conditions of use evaluated, such as pesticides and polyurethane foam applications, may not be current uses. For other uses, the use patterns and practices have likely changed to reflect better	Pesticides are not a chemical substance under TSCA and therefore outside the scope of this evaluation, which means that any pesticidal use of methylene chloride was not evaluated. Rather, EPA evaluated the processing of methylene chloride as a reactant (as an intermediate for pesticide, fertilizer, and other agricultural chemical manufacturing. See

	exposure control. EPA should consider reassessing the relevance of these uses that are no longer current.	section 5.2.1.3). EPA relied on reasonably available information throughout the risk evaluation process for use patterns and practices and, unless otherwise indicated in the evaluation, the conditions of use identified in the risk evaluation (e.g., industrial/commercial use as a propellent and blowing agent in polyurethane foam manufacturing) are considered intended, known or reasonably foreseen. These are conditions of use and are therefore evaluated in the risk evaluation.
77	**PUBLIC COMMENTS:** • EPA's identified conditions of use overlap, leading to internally inconsistent conclusions. EPA concludes that the industrial and commercial use of MC for paints and coatings presents an unreasonable risk, but simultaneously concludes that the distribution of MC in commerce does not present an unreasonable risk. • If EPA believes that only some uses of MC warrant regulation, such a determination is only appropriate at the Section 6(a) stage − not at the TSCA Section 6(b) stage, which charges EPA with the yes-or-no determination of whether a chemical presents an unreasonable risk.	TSCA section 6(b)(4)(D) requires EPA to conduct risk evaluations to determine whether a chemical substance presents unreasonable risk of injury to health or the environment, under the conditions of use. Therefore, TSCA section 6(b) risk evaluations can and should make unreasonable risk determinations for each condition of use included within the scope. While there may be connections between conditions of use, EPA distinguishes between them such that they do not overlap. Specifically, regarding the comment on distribution in commerce, for the purposes of the risk evaluation, distribution in commerce is the transportation associated with moving methylene in commerce. Unloading and loading activities are associated with other conditions of use. EPA assumes transportation of methylene chloride 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). Per the statute (see TSCA section 6(b)(4)(A)) and the implementing regulations for risk evaluations (40 CFR part 702, subpart B), EPA must make the unreasonable risk determination at the time of the risk evaluation. 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).
73	**PUBLIC COMMENTS:** • EPA did not address the presence of MC as a disinfectant byproduct in water as a condition of use. • EPA identified multiple on-topic literature sources addressing disinfection byproducts in the bibliography search results for MC	Methylene chloride generated as a byproduct of the disinfectant process for drinking water treatment is outside the scope of this risk evaluation. This activity would be considered in the scope of the risk evaluation for those drinking water treatment chemicals. EPA believes that its regulatory tools under TSCA section 6(a) are better suited to addressing any unreasonable risks that might arise from methylene chloride as a byproduct of the disinfectant process for drinking water treatment through

	but did not provide any rationale or scientific basis for excluding this condition of use. • As required by TSCA, EPA cannot exclude this condition of use based on its presence as a byproduct rather than being intentionally used.	regulation of the activities that generate methylene chloride as an impurity or cause it to be present as a contaminant than addressing them through direct regulation of methylene chloride. EPA expects that a risk evaluation of drinking water treatment chemicals would consider the requirements and existing regulations under the Safe Drinking Water Act as described in section 1.4.2.
79	**PUBLIC COMMENTS:** • [ ] reports a condition of use where MC is imported as part of a formulation. This proprietary blend, containing [ ] MC, is imported in drums for an industrial chemical customer in the United States [ ], which does not transfer material or otherwise open the imported drums, and ships the formulation in the original containers to the customer.	EPA appreciates the additional information regarding this specific importing scenario. In general, the occupational exposure scenario for import (which includes repackaging activities and exposures) is most suitable for the import of methylene chloride. Additionally, the scenario provided by the commenter is the distribution in commerce of methylene chloride, which is considered the transportation associated with the moving of methylene chloride in commerce with the unloading and loading activities associated with other conditions of use.
52	**PUBLIC COMMENTS:** • MC is used as a solvent for adhesive systems. The reported level of exposure workers using MC as a solvent for adhesive systems in commercial shops (p. 71) is likely incorrect because engineering controls can be too expensive for shops to install and proper PPE is often not worn.	EPA does not report a level of worker exposure on page 71. Page 71 covers releases to water and this is **not** associated with the worker exposure assessment.. EPA assesses adhesives and sealants use industrially and commercially in three sub-scenarios: spray, non-spray, and unknown application method. Monitoring data are used in each subscenario to estimate inhalation exposures, and modeling is used to estimate dermal exposures.
73	**PUBLIC COMMENTS:** • EPA does not explain why the finding of unreasonable risk would not equally extend to the distribution in commerce of MC as parts of these conditions of use. Distribution in commerce was not separately analyzed as parts of these conditions of use. • EPA assumes that distribution in commerce does not result in any exposures beyond those already related to a given	Distribution in-commerce is a distinct and separate condition of use. Some activities related to preparing the chemical or products for distribution, such as loading, unloading, and repackaging, are included in the relevant condition of use or evaluated separately (e.g. repackaging methylene chloride, Section 5.2.1.5). For the purposes of the unreasonable risk determination, distribution in commerce of methylene chloride is the transportation associated with moving methylene chloride in commerce. Unloading and loading activities are associated with other conditions of use. EPA assumes transportation of methylene chloride is in compliance with existing regulations for the transportation of hazardous materials, and emissions are therefore minimal (with the exception of spills and leaks,

	condition of use. EPA provides no analysis or evidence supporting this assumption. Is EPA assuming that all distribution occurs through "closed systems," which lead to no releases or exposure? EPA has provided no evidence indicating exposures and releases during distribution will be nonexistent.	which are outside the scope of the risk evaluation). Based on the limited emissions from the transportation of chemicals, EPA determines EPA's determination that there is no unreasonable risk of injury to health (workers and ONUs) from the distribution in commerce of methylene chloride.
28	**PUBLIC COMMENTS:** • Are exceptions to the rule being considered for academic labs, private industry, Biotech, Pharma, and manufacturers when appropriate engineering controls, work practices, and required personal protective clothing and equipment are used to prevent or reduce worker exposures below established Occupational Safety and Health Administration (OSHA) Permissible Exposure Limits (PELs), Short-Term Exposure Limits (STELs), etc.? • EPA should consider this comment in the rulemaking evaluation for the exemption for restrictions on the use of MC for certain industries.	EPA is unclear what the commenter means by "exceptions to the rule" and it appears the commenter may be referencing entities that could be subject to potential future risk management regulatory action. For purposes of estimating occupational exposures, based on the OSHA methylene chloride standard at 29 CFR 1910.1052, the only respirators that can be considered by EPA are supplied-air respirators (i.e., APF of 25 would be the lowest APF that could be considered), further discussed in section 2.4.1.1. As such, EPA assumes, as a baseline, the use of a respirator with an APF of 25. However, EPA is assuming that 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. EPA must evaluate the conditions of use it expects to consider under TSCA in the risk evaluation and propose risk management for any condition of use which the Agency determines presents unreasonable risk. Risk management activities will only occur after EPA has completed the risk evaluation. As the commenter indicated, for any condition of use determined to have unreasonable risk, EPA will consider this and other public comments during risk management.
65	**PUBLIC COMMENTS:** • The use of MC to manufacture pharmaceuticals is excluded from TSCA regulation and should not be within the scope of the risk evaluation.	While use of methylene chloride as a functional fluid in a closed system during pharmaceutical manufacturing was included in the problem formulation and draft risk evaluation, upon further analysis of the details of this process, EPA has determined that this use falls outside TSCA's

	• EPA should be explicit about what constitutes a chemical substance under TSCA. EPA may not regulate non-TSCA uses in a risk management rule under Section 6(a). • Neither the problem formulation, nor the prior scope document, nor the draft risk evaluation, discusses the fact that MC's use in pharmaceutical manufacture is a non-TSCA use. • EPA is obligated to revise the draft risk evaluation to exclude all discussion of MC's use in pharmaceutical manufacturing – except to explain the basis for its exclusion.	definition of "chemical substance." 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 found that methylene chloride use as a functional fluid in a closed system during pharmaceutical manufacturing entails use as an extraction solvent in the purification of pharmaceutical products, and has concluded that this use falls within the aforementioned definitional exclusion and is not a "chemical substance" under TSCA (section 5.3)
Consideration of exposure from accidental release		
73, 72	**PUBLIC COMMENTS:** • The draft risk evaluation and problem formulation do not consider potential releases and exposures resulting from accidental releases which should be considered to be "reasonably foreseen", particularly in cases of flooding, and other natural disasters.	Releases from accidents Releases from accidents generally are not included within the scope of a TSCA risk evaluation. First, EPA does not identify accidental releases as "conditions of use." EPA does not consider MC releases from accidents to constitute circumstances under which MC 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 MC is manufactured, processed, distributed, used, or disposed of to include uncommon and unconfined releases from accidents for purposes of the statutory definition. Further, EPA does not generally consider accidental releases to constitute "disposal" of a chemical for purposes of identifying a COU in the conduct of a risk evaluation. In addition, even if accidental releases of MC could be considered part of the listed lifecycle stages of MC, EPA has "determined" that such releases are not circumstances under which MC 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 to exclude releases from accidents from the scope of the MC 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 accidental releases as part of the risk evaluation, which could make the conduct of the risk evaluation untenable within the applicable deadlines, MC releases from accidents are determined not to be circumstances under which MC 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 MC releases from accidents 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 accidental releases, 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 MC releases from accidents to be COUs. Second, even if MC releases from accidents 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, exclude certain activities that EPA has determined to be conditions of use 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...." The approach discussed in the Risk Evaluation Rule and applied in the problem formulation documents 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). Following coordination with EPA's Office of Land and Emergency Management (OLEM), EPA has found that exposures of methylene chloride from accidental spills 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 methylene chloride as hazardous waste no. U080). As a result, EPA believes it is both reasonable and prudent to tailor the TSCA risk evaluation for methylene chloride by declining to evaluate potential exposures from accidental releases, rather than attempt to evaluate and regulate potential exposures from accidental releases under TSCA. <u>Releases from floods/natural disasters</u> For the same reasons noted above, releases of MC from floods and natural disasters were not included within the scope of the MC risk evaluation. EPA does not identify releases from floods and other natural disasters as "conditions of use." Based on the circumstances surrounding chemical releases from floods and natural disasters, which are uncommon and

		outside the control of regulated entities or other persons, EPA does not consider such acts to be reasonably viewed as known, intended, or reasonably foreseen forms of chemical manufacture, processing, distribution, use, or disposal. In particular, EPA does not consider an uncommon and uncontrolled event like a flood or natural disaster to be a "probable" part of the chemical lifecycle described in the definition of "conditions of use," and believes this is a reasonable approach to meaningfully limit activities within the scope of EPA risk evaluations. In addition, even if releases of MC from floods or natural disasters could be considered part of the listed lifecycle stages of MC, EPA has "determined" that MC releases from floods and natural disasters are not circumstances under which MC 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 to exclude releases of MC from floods or natural disasters from the scope of the MC risk evaluation. For instance, an analysis of natural disasters like floods could entail evaluation primarily on the basis of skewed exposure assumptions and the chemical's hazards (e.g., an assumption of 100% chemical release, resulting in theoretical, maximal exposure to any nearby populations), contrary to what might be contemplated for evaluation of a condition of use under TSCA section 6(b)(4)(F). EPA does not believe that Congress intended the Agency to evaluate circumstances such as natural disasters where the evaluation would cover only half of the risk calculation (hazard but not exposure) for the scenario at issue. Exercising the discretion to not identify releases of MC from floods and other natural disasters 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 2(c), 3(4), 3(12), 6(b)(4)(D), 6(b)(4)(F). For these reasons, EPA is exercising this discretion to not consider floods and other natural disasters to be COUs of MC.

		Second, even if MC releases from floods or other natural disasters could be identified as a COU, or a form of exposure from a COU, in some cases, these are not COUs or exposures that EPA "expects to consider" in the MC risk evaluation per TSCA section 6(b)(4)(D), and EPA is exercising its authority under TSCA to tailor the conditions of use and exposures evaluated in the MC risk evaluation. Given the rare , unpredictable, and uncontrollable nature of floods and other natural disasters, EPA does not believe that Congress intended the Agency to evaluate such acts during TSCA risk evaluation.
Exclusion of exposure pathways subject to other regulation		
33, 42, 44, 70, 73, 76, 77	**PUBLIC COMMENTS:** • "EPA plans to exclude exposure pathways for methylene chloride that allegedly are addressed under other statutes although these pathways have been identified for regulation precisely because they are known or suspected to pose a serious concern…" • EPA excludes all general population risks arising from exposures from releases to land, air, and water based on the assumption that other statutes adequately address the exposures i.e., the Clean Air Act ("CAA")" (p. 428). • EPA has failed to provide any scientific rationale for this assumption and this strays from basic risk assessment principles by omitting well known exposure routes such as water consumption by all occupationally and non-occupationally-exposed humans as well as similar exposures to other biological receptors. • The problem formulation included less than four pages to justify EPAs decision to eliminate entire pathways and provided no data or analysis of the exposures and risks	Clarifying language about what pathways are addressed under other statutes has been added to Section 1.4.2 of the Risk Evaluation.

	that remain and their contribution to total exposure and risk. The draft risk evaluation provided no additional analysis. See MC problem formulation pp. 54-57 and the draft risk evaluation p. 33.	
44, 73	**PUBLIC COMMENTS:** • EPA has excluded environmental releases from its risk determinations. Due to its exclusion of all exposures via environmental releases to air, water, and land, EPA has not considered all non-occupational baseline exposures workers experience. The agency needs to take these into account as baseline exposures for workers.	EPA did not consider background exposure that workers and consumers using products containing MC might be exposed to in addition to exposures from TSCA-regulated conditions of use. This may result in an underestimation of risk, and additional discussion of this underestimation has been added to the document in the uncertainties section 4.3.2 for occupational exposure. Additionally, clarifying language about what pathways are addressed under other statutes has been added to Section 1.4.2 of the Risk Evaluation.
Need to aggregate exposure/risk across conditions of use		
44, 49, 66, 72, 73, 75, 77	**PUBLIC COMMENTS:** • EPA failed to assess "the combined exposures to an individual from a single chemical substance across multiple routes and across multiple pathways" which contravenes EPA's mandate under TSCA Section 6(b). • This includes risk from aggregate exposures such as concurrent workplace, consumer product, and environmental exposures, which are common occurrences for many individuals and communities. • EPA acknowledges, "[s]ome products [containing methylene chloride] are used in both commercial and consumer applications such as adhesives and sealants"; however, EPA did not conduct a	• 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 for the aggregate exposure, 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 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 the Key Assumptions and Uncertainties section describing these assumptions and uncertainties. • EPA did not consider background exposure that workers and consumers using products containing MC might be exposed to in addition to exposures from TSCA-regulated conditions of use. This may result in an underestimation of risk, and additional discussion of

	cumulative risk assessment taking this information into consideration. • EPA is not authorized to identify particular conditions of use and make individualized determinations as to whether each condition of use, rather than each chemical, presents an unreasonable risk. • TSCA requires EPA risk evaluations to "describe whether aggregate or sentinel exposures to a chemical substance under the conditions of use were considered, and the basis for that consideration." The MC draft indicates that EPA used an "aggregate exposure" methodology by estimating dermal and inhalation risks for each condition of use (even though it failed to combine them) but ignores the possibility of concurrent exposure to MC across conditions of use. • EPA is not authorized to identify particular conditions of use and make individualized determinations as to whether each condition of use, rather than each chemical, presents an unreasonable risk. • Aggregation of multiple pathways that contribute to individual exposure would result in even smaller margins of exposure (MOEs) for acute and non-cancer chronic effects and larger carcinogenicity risks under MC's conditions of use.	this underestimation has been added to the document in the Key Assumptions and Uncertainties section. • 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." • 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 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.

		• EPA did not consider background exposure that workers and consumers using products containing MC might be exposed to in addition to exposures from TSCA-regulated conditions of use. This may result in an underestimation of risk, and additional discussion of this underestimation has been added to the document in the Key Assumptions and Uncertainties section.
Occupational exposure estimates – vapor degreasing		
45, 66	**PUBLIC COMMENTS:** • Regarding the open top vapor degreasing scenario (p. 123), EPA had no monitoring data and thus performed modeling of near-field and far-field exposure concentrations. It may be possible to use surrogate data and correct for vapor pressure and vapor density using data from other common solvents to add to the empirical validation of the model estimates. • Some of the data are of limited quality; for example, p. 374: "The emission rate for conveyorized vapor degreasing is based on equipment at a single site and the emission rates for web degreasing are based on equipment from two sites. It is uncertain how representative these data are of a 'typical' site."	Because MC-specific emission rates were available for modeling of open top vapor degreasing, EPA did not pursue modeling for this use using surrogate data for other chemicals. Such surrogate modeling would unnecessarily add additional uncertainties that would prevent usefulness toward validation. Regarding the limited data for conveyorized and web degreasing, the limited number of sites does not impact data quality but does impact representativeness. This impact on representativeness is noted as an uncertainty in section 4.3.2.2.1.
Occupational exposure estimates – cold cleaning		
45, 68, 56	**PUBLIC COMMENTS:** • For cold cleaning (p. 125), the exposure estimates based on historical data versus the model were very different (280-fold for the central tendency estimate). EPA ultimately chose the central tendency estimate based on monitoring. This specific value was chosen because EPA did not have underlying data, rather only a	EPA has added explanation to section 2.4.1.2.7 to explain that monitoring data have higher weight of evidence due to higher relevance than modeling results for this use for several reasons: (1) monitoring data are known to be relevant to this use; and (2) the modeled results cannot be validated and do not capture the full range of possible exposure concentrations identified by the monitoring data for this use. For example, the 95th percentile modeling results appear equal to about the 25th percentile of monitoring data. Also, EPA uses

	reported air concentration range of 14-1,000 mg/m3, as reported by TNO (CIVO) 1995. This difference in estimated exposure, and the resulting choice made by EPA to use the measured yet uncertain and old monitoring data, represent the selection of hierarchy rather than weight-of-evidence (WOE) approaches. Methods should be informed by both the empirical data and models – not individually in a hierarchy. • For the cold cleaning occupational condition of use, EPA utilized inhalation data from the published literature dating to 1998. These data were rated as low quality, in line with EPA's systematic review guidelines, yet EPA also ran Monte Carlo simulations for this condition of use, arriving at values that differed by an order of magnitude (Section 2.4.1.2.7, p. 126). • Despite the published data's low-quality, EPA used these because the modeled data "[did] not capture the full range of possible exposure concentrations identified by the monitored data." It is not clear from the draft risk evaluation what ranges EPA believes the monitored data captured that the modeled data did not. Further, given the available inputs in the Monte Carlo model, EPA does not explain why this model could not accommodate these ranges, or how it came to the conclusion to use low quality monitoring data.	the occupational exposure data with the highest quality rating, and sometimes the highest quality data available have a low quality rating.
Occupational exposure estimates – manufacturing, reactant, processing		
SACC	**SACC COMMENTS:**	• EPA added text to Section 2.4.1.2.15 of the Risk Evaluation and Section 2.15.3.2 of the Supplemental Information on Releases and

	• The exposure concentrations for polyurethane foam manufacturing are highly variable (Tables 2-65 and 2-66). Therefore, a clearer presentation of resulting uncertainty in exposure estimates is important.	Occupational Exposure Assessment to discuss variability in exposure concentrations for polyurethane foam manufacturing.
SACC	**SACC COMMENTS:** • The Committee was concerned about how the risk evaluation characterizes occupational inhalation exposure of MC as used in manufacturing (domestic manufacture), processing (as a reactant) distribution, industrial, and commercial use as a laboratory chemical for all other chemical product and preparation manufacturing.	EPA takes note of the SACC concerns about these conditions of use. EPA has described the risks and its assumptions and uncertainties. It has provided additional justification for using high-end exposure estimates in its upper bound risk estimation
66	**PUBLIC COMMENTS:** • Although exposure data were used to calculate 8-hour time-weighted averages (TWAs) for manufacturing (p. 114), processing as a reactant (p. 116), and processing (p. 118), the data are very limited and most likely not representative of true exposure. For instance, for manufacturing only data from one facility was provided, and for processing, only data from two facilities were given.	EPA states the uncertainty of representativeness as a primary uncertainty for each occupational exposure scenario that includes monitoring data and in the Uncertainties section 4.3.2. EPA has also obtained additional monitoring data from OSHA to bolster the monitoring data base for many COUs.
66, 68, 75, 49, 72, 73	**PUBLIC COMMENTS:** • EPA inappropriately relies solely on occupational exposure data from the Halogenated Solvents Industry Alliance (HSIA) for two conditions of use and ignores available data from OSHA to support its determinations of no unreasonable risk. • Dr. Adam Finkel provided information to	• EPA used the highest quality data reasonably available for all scenarios, including the HSIA data. EPA consulted with and obtained data from OSHA, whose data are used and cited in the Risk Evaluation as OSHA, 2019. EPA added pretreated 8-hr TWA data from Dr. Finkel into the exposure assessment in 12 occupational exposure scenarios (OESs). The new data added for each OES ranged from 12 to 468 points. The Commercial Aerosol Products OES previously had only modeling but now has monitoring data as well.

	EPA on 12,152 air samples that OSHA collected on MC. EPA references only 15 of those samples (<0.2%) in its draft risk evaluation, solely for the spot cleaning and fabric finishing conditions of use. • EPA does not explain why the remaining data in Dr. Finkel's submission (which received a "medium" data quality score in EPA's systematic review) were not used. Nor does EPA address whether OSHA was in possession of additional MC monitoring data and, if so, explain why it did not contact OSHA directly to request access. EPA made no effort to compare the HSIA data with the air samples submitted by Dr. Finkel or other monitoring data for the two conditions of use in the possession of OSHA or state agencies. • HSIA is the main trade association for manufacturers of MC, and, as such, it has a strong vested interest in EPA finding no unreasonable risk from the chemical. It appears to be a lobbying group. This calls into question the reliability and completeness of the data voluntarily submitted by HSIA. • For the manufacturing of MC and the processing of MC as a reactant, EPA relied exclusively on exposure data from three facilities provided by the HSIA. 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.	The Adhesives and Sealants OES has a new Unknown Application Method subcategory (added to Spray and Non-spray categories) • HSIA data were provided as part of continuous IH monitoring programs and were evaluated using the same criteria as all other data sets. The only other reasonably available data readily attributable to manufacturing and processing of MC were limited and contained their own deficiencies, such as the age of the studies, lack of discrete data points, and no metadata information, resulting in low quality ratings. • 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 1.4.4.4 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 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 used all 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.

	• EPA is mandated under TSCA to consult with OSHA. In finalizing the MC risk evaluation, EPA should make every effort to obtain additional workplace monitoring data from OSHA, state agencies, and industry and should use all data in its possession to determine unreasonable risks to workers. • Descriptions of discussions and consultation with OSHA should be documented and included in the risk evaluation.	
Occupational exposure estimates – pharmaceutical production		
45, 65	**PUBLIC COMMENTS:** • The draft risk evaluation cites a World Health Organization (WHO) publication for MC exposures in the pharmaceutical manufacturing industry. The WHO publication (1996b) is actually a secondary reference that in turn cites Zahm et al. (1987) and HSE (1992). Zahm (1987) reports MC exposures that range from 7.1 to 3749 mg/m^3 (on an 8-hour TWA basis) and it appears that these data were used by EPA in its risk calculations. The Zahm (1987) report is very old and based on metadata collected at a time when pharmaceutical manufacturing was often done in open vessels. That is no longer the case, and thus, data from Zahm (1987) are not representative of current practices. Further, the dermal estimate is flawed, as gloves would be worn for product quality. • Under EPA's TSCA systematic review guidance, these data should be rated "low" for the temporality metric of	• EPA has removed assessment of Pharmaceutical Production from the risk evaluation because this use is not a TSCA use.

	representativeness (>15 years old). They should not be used for exposure assessment, particularly when more timely (and thus more representative) data are available. • In contrast to Zahm (1987), the other primary source discussed in the WHO study – HSE (1992) – reported MC exposure data from pharmaceutical manufacturing (0-18 mg/m^3, 8-hour TWA) that are consistent with recent data provided to EPA. EPA should thus rely on this study, and not Zahm (1987), in its final risk evaluation. • A comparison of recent data (from a modern pharmaceutical manufacturing site) to the data used by EPA in its draft risk evaluation was made, and there was no instance in which current exposure levels exceeded EPA de minimis risk levels or the PEL (25 ppm = 86.8 mg/m^3).	
Occupational exposure estimates – waste handling		
66	**PUBLIC COMMENTS:** • Very few exposure data are available for waste handling. The available data might not truly represent worker exposure concentrations (p. 160). Three data points are not enough to make a statistical determination of exposure (p. 161).	As stated in the first 10 Draft Risk Evaluations, EPA makes statistical estimates of 50th and 95th percentiles for exposure scenarios with 6 or more data points, and this scenario has 22 full shift data points. The uncertainty of representativeness is included as a primary uncertainty towards confidence in the section 2.4.1.2.21 covering Waste Handling, Disposal, Treatment, and Recycling.
Occupational exposure estimates - repackaging		
45	**PUBLIC COMMENTS:** • When historical data were used, it is sometimes unclear whether the source reported the associated exposure conditions, including the use of personal protective equipment and local exhaust	EPA has clarified in section 2.4.1.2 that EPA could not determine whether PPE or engineering controls were used for some settings where monitoring was conducted.

	ventilation (e.g., in the repackaging use with the 1976 Unocal data from an American Industrial Hygiene Association (AIHA) report (p. 120).	
Occupational exposure estimates – painting and coating		
45	**PUBLIC COMMENTS:** • The painting and coating industrial hygiene data demonstrate how variable the data are among studies and applications, emphasizing the role of local scenario factors (p. 132). As such, there are questions regarding whether these data are sufficiently representative for decision-making.	Such data variability are common in many OESs, and EPA believes that data variability may improve representativeness. EPA has been transparent about the uncertainty of representativeness towards confidence in each OES section of 2.4.1.2 and overall in the Uncertainties section 4.3.2.1.
Near-field wind speed and use of ventilation in estimating occupational inhalation exposure		
SACC	**SACC COMMENTS:** • Clarify the issues related to near-field air wind speed and use of additional ventilation in the scenario. o It is unclear from the text of the report why the near-field indoor air speed is not related to the air exchange rate and the volume of the room. o It is also unclear why the speed of air movement in the near-field would not be the same as for the rest of the room unless some type of additional ventilation (i.e., a fan) was used in the near-field. The use of additional ventilation was not mentioned in the text. o It is also unclear why movement of the chemical in the air was modeled using air speed rather than diffusion between the near-field and far-field. **PUBLIC COMMENT:**	• There is no additional ventilation (e.g., fan) modeled in this scenario. The scenario is as described in Figure F-1. Air does not necessarily move through a workplace in plug flow. While the air exchange rate (and air volumetric flow rate) is a function of the ventilation system's air moving capacity, the air speed is a function more of the configuration of the air ventilation system, moving or rotating equipment that may cause air currents, and the movement of people. Air moves in multiple, swirling directions with variations in localized air speeds. Workplaces are generally expected to have turbulent air flow, with air moving in turbulent eddy currents. While air speed can vary spatially depending on the geometry, configuration, and placement of equipment and other objects in the workspace, the model uses a mean air speed. This is the mean air speed throughout the workplace and is modeled using a distribution derived from the mean air speeds calculated by Baldwin and Maynard (1998) based on their measured air speeds in workplaces. Therefore, the model uses a single value of air speed for the near-field and far-field (this value varies from iteration to iteration following its distribution).

	• None of the exposure estimates (including modelled scenarios) considered the use of active ventilation controls. This is a major limitation that likely yields significant overestimates of exposure. Consideration of modern handling practices and presence of engineering controls (e.g., ventilation) can be built into modeling scenarios.	Under these circumstances, diffusion is a weak form of mass transfer compared to convection. If we were to approximate the Peclet number for the near-field, using the NF's radius (1.5 m), the median mean air speed (8.78 cm/s), and an approximate diffusivity of water vapor in air (0.282 cm^2/s), we calculate a Peclet number of approximately 4,700. Since this number is orders of magnitude greater than one, this confirms that convection is of much greater importance than diffusion to mass transfer. A more rigorous approach would use computational fluid dynamics (CFD) to discretize the workplace volume and solve the mass and momentum balances, calculate the various length scales of the eddy currents, and calculate local Peclet numbers. Higher energy eddy currents are expected to show convection (or turbulent "diffusivity") more important than molecular diffusion. As eddy currents dissipate energy and become smaller, there may be small length scales (i.e., Kolmogorov microscale) where molecular diffusion becomes more important. These domains are of negligible importance to the overall mass transfer of chemical through the workplace.
Characterization of important exposure determinants in occupational exposure assessment approach		
SACC	**SACC COMMENTS:** • Provide a better characterization of important exposure determinants (i.e., number of tasks/occupations, number of companies sampled, date range of samples, conditions under which measurements were taken) when describing the exposure data and exposure assessment approach in the occupational exposure scenarios in Section 2.4.1.2 of the risk evaluation. • The mathematical approach used to estimate the central tendency and high-end percentiles when the distribution of exposure samples is unknown does not account for all sources of variability in exposure, nor does it account for representativeness of exposure estimates	EPA has added these important exposure determinants when known. Full details of available data are in Appendix A of the Supplemental Information on Releases and Occupational Exposure Assessment. Representativeness of data is discussed in Section 4.3.2.1 of the Risk Evaluation and Section 4.2.2 of the Supplemental Document.

	within each occupational exposure scenario. • For example, the data provided by the HSIA for worker exposure during manufacturing (Tables 2-28 and 2-29) are based on 136 samples, coming from only 2 companies.	
Occupational exposure estimates – general		
SACC	**SACC COMMENTS:** • Possible values of Fabs should be discussed when this parameter is first defined in the text. This is typically done for a number of the other parameter values.	• EPA has added discussion to Key Dermal Exposure Dose Models section of Section 2.4.1.1 in the Risk Evaluation to include the possible values of Fabs and reference to the Supplemental Information on Releases and Occupational Exposure Assessment for more details.
SACC	**SACC COMMENTS:** • EPA should not refer to the 95th percentile value as a 'high-end estimate' of exposure. It is misleading to suggest that the 95th percentile value is an upper bound on exposure since exposure distributions are typically skewed and as a result, higher percentile values (e.g., the 99th percentile value) can often be an order of magnitude or higher than the 95th percentile value.	• EPA has included in 2.4.1.1 the definition of the term "high-end" taken from EPA's Guidelines for Exposure Assessment (HERO 90324) and shown in the Supplemental Information on Releases and Occupational Exposure Assessment. These Guidelines define high-end as an exposure value above the 90th percentile but below the exposure of the individual with the highest exposure. The Guidelines also recommend not using higher values in the high-end, such as 98th or higher. EPA does not suggest or use the term "upper bound."
SACC	**SACC COMMENTS:** • SACC indicated the need to determine and describe occupational exposure scenarios where the industry standard is to provide dedicated ventilation.	While EPA has learned of some exposure scenarios where dedicated ventilation was in use, EPA did not find reasonably available information to determine and describe occupational exposure scenarios where the industry standard is to provide dedicated ventilation.
73	**PUBLIC COMMENTS:** • In its systematic review process, EPA rated the 2018 HSIA data as 1.6, or "High." However, it appears that the data represent only four manufacturing facilities and it is unclear how representative of the entire country the data are.	EPA states the uncertainty of representativeness which is included as a primary uncertainty towards confidence in section 2.4.1.2.1 covering Manufacturing. EPA estimates between 4 and 14 sites for this COU. EPA does not believe that its weighting criteria for occupational exposure data are inconsistent with best practices in systematic reviews.

	• EPA's approach to weighting criteria, which is inconsistent with best practices in systematic reviews, results in the "Low" Methodology score for the 2018 HSIA having little impact on its overall score. • EPA's systematic review protocol does not take into consideration the potential for bias based on the data source. • EPA provides insufficient justification for its exclusive reliance upon this potentially biased data without independent validation and quality assurance reporting.	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 HSIA data are the highest quality data for two COUs. Independent validation of data is not available for these COUs.
49, 72	**PUBLIC COMMENTS:** • EPA determined that MC presents no unreasonable risk without considering the vast majority of that data. In so doing, EPA violated its statutory obligation to consider "reasonably available information" when evaluating chemical risks. • EPA fails to consider readily available data on occupational exposures to MC, and thus lacks sufficient information to support its proposed determinations of no unreasonable risk.	EPA has considered all reasonably available data on occupational exposures to MC. Some data did not have sufficient metadata such as more specific industry codes and worker activities needed for incorporation in the risk evaluation. When sufficient metadata is not reasonably available, EPA cannot utilize the underlying dataset. For example, some data do not have the metadata to associate it with a particular industry or use or to associate it with a particular time averaging. EPA has added hundreds of additional data pointsfrom previously underutilized sources of OSHA data.
Occupational exposure estimates – combining pre and post OSHA PEL (1997)		
SACC, 41, 45, 65, 67	**SACC COMMENTS:** • The risk evaluation groups MC area and exposure measurement data pre- and post-revision of the PEL from 500 to 25 ppm in 1997, which could lead to overestimation of exposure. • The analysis of these OSHA inspection data suggests that exposure levels did not change dramatically before and after 1997, so that the data could be combined for the purpose of exposure estimation.	In section 4.3.2.1, EPA states the uncertainty of the use of data from before the PEL revision and that use of some older data may overestimate some exposures. EPA revised text in 2.4.1.1 to expand upon adequacy of older data and summarize EPA's new statistical analysis, which is included as a new appendix in the Supplemental Information on Releases and Occupational Exposure Assessment. EPA added text to 2.4.1.1 noting that some producers and users of MC may have started implementing changes before the PEL revision became effective, which could also be a factor in the relatively limited reduction in exposures between the pre- and post-revision of the PEL periods. EPA analyzed 8-hr TWA exposures measured prior to April 10, 1997 (pre-rule) and after April 10, 2000 (post-

	• The statement that "…incremental general exposure reductions due to the PEL change…" indicate that "…exposure data from before the PEL are adequate" (Section 2.4.1.1, p. 108, lines 1852-1854) needs to be expanded. • The argument for combining the two periods could be strengthened by an expanded discussion of the mix of products, processes, and/or worker practices before and after 1997, about which EPA claims to not have received information. It is not clear whether EPA contacted users proactively to obtain this information. • It is likely that producers and users of MC started implementing changes before 1997, in advance of the expected promulgation of the 25 ppm PEL. This could also contribute to explain the relatively limited reduction in exposures between the two periods. • The Committee noted that data collected after the PEL should simply be given more weight.	rule), respectively. Several distributional statistics showed consistent reductions of about 30% to 35% following a reduction in the PEL of 95%. Hence, a twentyfold reduction in the PEL resulted in only an approximately 1.5-fold reduction in actual exposures. Due to the small reduction in exposures relative to the reduction in PEL, EPA included the pre-rule samples in the occupational exposure assessment to provide a more robust data set. While EPA's new analysis justifies the use of the pre-PEL change data, EPA weighted use of pre-PEL change data through changes in overall confidence ratings. Strength of overall confidence in monitoring data is reduced depending upon the reliance of use of monitoring data that had been sampled before the OSHA PEL for methylene chloride was reduced (effective after transition in 2000).
SACC	**SACC COMMENTS:** • Analyze the OSHA data using appropriate statistical methods for each use category and cite the results to justify that the old monitoring data remains relevant for assessing exposures in 2019.	EPA revised text in 2.4.1.1 to summarize EPA's new statistical analysis, which is included as a new appendix in the Supplemental Information on Releases and Occupational Exposure Assessment. The new analysis uses appropriate statistical methods and shows changes in exposures for each use category for which data are available. EPA found a range of exposure reductions across eight industry sectors and increases for two sectors. The largest decreases were for spot cleaning (94.5%), fabric finishing (93.4%), and use of adhesives (50.6%). On the other hand, exposures increased for plastics manufacturing (617%) and aerosol degreasing (130%). The results justify use of the pre-PEL change data but with lower weight in some use categories. EPA weighted use of pre-PEL change data through

		changes in overall confidence ratings. Strength of overall confidence in monitoring data is reduced by having a portion of a use's monitoring data that had been sampled before the OSHA PEL for methylene chloride was reduced (effective after transition in 2000).
Data quality of Finkel (2017) commentary		
45	**PUBLIC COMMENTS:** • EPA did not assess the methodological validity or reliability of the Finkel (2017) commentary, which was critical to assumptions in the risk evaluation.	EPA assessed the analysis in Dr. Finkel's commentary to determine potential improvements. EPA revised text in 2.4.1.1 to summarize EPA's new statistical analysis, which is included as a new appendix in the Supplemental Information on Releases and Occupational Exposure Assessment. The new analysis has improvements in validity and reliability than the analysis in the commentary. For example, EPA's analysis excluded samples that were not personal samples or had unit of measure denoted "X" or were blank, and apparent duplicate samples. EPA also combined samples with the same sample number (but different values of sample time and sample result), which were assumed to be samples taken on the same worker to calculate an 8-hr TWA. EPA investigated and found that the analysis is not sensitive to values of the level of detection used.
Concerns with Finkel analysis of pre- and post-1997 occupational exposure data		
67, 45	**PUBLIC COMMENTS:** • Several public commenters summarized Finkel's letter comparing airborne occupational MC concentrations pre- and post- implementation of the 1997 OSHA standard. Two of the commenters pointed out limitations of his analysis including: a lack of transparency in the dataset (i.e., not publicly available, not from an identifiable peer-reviewed source, durations were not provided, missing units of measurement). All exposure concentrations should be converted to the same unit of measure for appropriate comparison. There is also uncertainty whether compliance-driven data that is not randomly sampled adequately	EPA assessed the analysis in Dr. Finkel's commentary to determine potential improvements. EPA revised text in 2.4.1.1 to summarize EPA's new statistical analysis, which is included as a new appendix in the Supplemental Information on Releases and Occupational Exposure Assessment. EPA's new analysis supersedes and replaces the Finkel analysis and has improvements in validity and reliability and uses appropriate statistical methods. For example, EPA's analysis excluded samples that were not personal samples or had unit of measure denoted "X" or were blank (thereby using the same unit of measure), and apparent duplicate samples. EPA also combined samples with the same sample number (but different values of sample time and sample result), which were assumed to be samples taken on the same worker to calculate an 8-hr TWA. EPA investigated and found that the analysis is not sensitive to values of the level of detection used. Also, EPA analyzed by NAICS codes to show differences among industry classes. The new analysis shows changes in exposures for each use category for which data are available. EPA found a range of exposure reductions across most industry

	represent the full range of exposure, and there is lack of appropriate statistical analysis to support his claim. Specifically, it is clear that the data do not approximate a normal distribution (i.e., do not fall closely along the centerline on the probability plot); therefore, any statistical comparisons should be made using transformed data with comparison between the geometric, rather than arithmetic means. This allows more weight to be placed upon the majority of the data that falls at lower concentrations. • A commenter suggested EPA re-assess the use of Finkel's analysis for the risk evaluation, because he grouped all available OSHA personal monitoring data from MC to calculate trends without stratification by different uses/scenarios, and OSHA data are not representative of the industry as a whole.	sectors and increases for several sectors. The largest decreases were for spot cleaning (94.5%), fabric finishing (93.4%), and use of adhesives (50.6%). On the other hand, exposures increased for plastics manufacturing (617%) and aerosol degreasing (130%). The results justify use of the pre-PEL change data but with lower weight in some use categories. EPA weighted use of pre-PEL change data through changes in overall confidence ratings. Strength of overall confidence in monitoring data is reduced by having a portion of a use's monitoring data that had been sampled before the OSHA PEL for methylene chloride was reduced (effective after transition in 2000). These OSHA data are adequately representative to use for this analysis.
67	**PUBLIC COMMENTS:** • Cardno ChemRisk performed a de novo analysis of the publicly available OSHA dataset. This included a review of all field definitions. The differences observed in this simplified analysis illustrate the importance of proper data subsetting when analyzing the appropriateness of empirical data for exposure estimation. • Overall, the Cardno ChemRisk evaluation concluded that there is indeed a reduction in MC exposures before and after the implementation of the OSHA standard, and that this difference was statistically	EPA assessed the analysis by Cardno to determine potential improvements. EPA revised text in 2.4.1.1 to summarize EPA's new statistical analysis, which is included as a new appendix in the Supplemental Information on Releases and Occupational Exposure Assessment. EPA's new analysis has improvements in validity and reliability and uses appropriate statistical methods. For example, EPA's analysis excluded samples that were not personal samples or had unit of measure denoted "X" or were blank (thereby using the same unit of measure), and apparent duplicate samples. EPA also combined samples with the same sample number (but different values of sample time and sample result), which were assumed to be samples taken on the same worker to calculate an 8-hr TWA. EPA investigated and found that the analysis is not sensitive to values of the level of detection used. Also, EPA analyzed by NAICS codes to show differences among industry

	significant. In addition to a significant lowering of workplace exposures as a result of the OSHA Standard, there were also significant differences in the reported exposure values across business types when the OSHA dataset was separated by NAICS code. Aggregating the data from all commercial/industry uses, as done in the Finkel report, increased the overall variability in the dataset, thus reducing the ability to detect any trends by industry or date. • EPA should consider re-evaluating the appropriateness of its use of aggregated historical data and increase emphasis on recent exposure monitoring data supplemented by model estimates for the revised risk evaluation.	classes. EPA re-evaluated and confirmed the appropriateness of its use of aggregated historical data using a new analysis. The new analysis uses appropriate statistical methods and shows changes in exposures for each use category for which data are available. EPA found a range of exposure reductions across most industry sectors and increases for several sectors. The largest decreases were for spot cleaning (94.5%), fabric finishing (93.4%), and use of adhesives (50.6%). On the other hand, exposures increased for plastics manufacturing (617%) and aerosol degreasing (130%). The results justify use of the pre-PEL change data but with lower weight in some use categories. EPA weighted use of pre-PEL change data through changes in overall confidence ratings. Strength of overall confidence in monitoring data is reduced by having a portion of a use's monitoring data that had been sampled before the OSHA PEL for methylene chloride was reduced (effective after transition in 2000). EPA has exhausted all modeling opportunities with the data that are reasonably available.
Approach to handling non-detect values in exposure measurements		
SACC, 67	**SACC COMMENTS:** • A Committee member pointed that there are different approaches for handling non-detect values beyond replacement by ½ the detection limit, 0, or the detection limit. The selection of non-detect replacement method can affect estimates of central tendency and 95th percentiles. • A substantial body of literature on the treatment of non-detects for estimating population parameters has been developed including studies and guidance by EPA. The EPA should consider these methods. As a start, Helsel (2010) provides a critical review of some methods for dealing with non-detects. **PUBLIC COMMENTS:**	EPA used its documented approach for occupational exposure data that were reported as below the limit of detection. This approach has been used consistently across the Risk Evaluations and is summarized in section 1.4.4.2 of the Supplemental Information on Releases and Occupational Exposure Assessment. For datasets including exposure data that were reported as below the limit of detection (LOD), EPA estimated the exposure concentrations for these data, following EPA/OPPT's Guidelines for Statistical Analysis of Occupational Exposure Data (1994) which recommends using the LOD / $2^{0.5}$ if the geometric standard deviation of the data is less than 3.0 and LOD / 2 if the geometric standard deviation is 3.0 or greater (EPA, 1994). For environmental and consumer exposures, limits of detection were reported as stated within the evaluated reviewed literature and evaluated monitoring information. As explained, those limits of detection varied amongst studies based on differences in sampling routine, methodology, and precision in available analysis tools. No values using relevant limits

	• The dataset did not report the limit of detection (LOD) associated with each of the samples. Without the actual analytical limits of detection, a substitution for the limit of detection (such as LOD/SQRT(2)) is not feasible. • The ProUCL 5.1 User Guide (Singh and Maichle, 2015), and Regression on Order Statistics (ROS) methods are used to fill in non-detect values in alignment with the lognormal distribution as determined from the non-censored concentrations.	of detection were incorporated into the consumer or environmental modeling outputs.
Occupational exposure comparisons to PEL		
67	**PUBLIC COMMENTS:** • In 1997, OSHA lowered the workplace exposure limit for MC from 500 to 25 ppm as an 8-hour TWA. In addition, it established a STEL (15-minute) of 125 ppm and an action level for concentrations of airborne MC of 12.5 ppm (8-hour TWA) resulting in a 95% reduction in acceptable exposures. • There is no basis for EPA to assume that MC is being used at levels that would be in violation of the OSHA standard. Nevertheless, the draft risk evaluation uses incorrect baselines for exposure to MC, particularly the occupational exposure scenarios.	This OSHA workplace exposure limit reduction is noted in section 2.4.1.1 of the risk evaluation. Reasonably available data indicates that exceedances of the limits can occur in some scenarios. EPA is not aware of any incorrect baselines.
73	**PUBLIC COMMENTS:** • The current draft risk evaluation does not mention EPA's 2017 recommended Existing Chemical Concentration Limit (ECEL). • If EPA were to compare its workplace exposure estimates to the ECEL – as	EPA did not recommend this ECEL in the 2017 proposed rule for methylene chloride in paint and coating removal (82 FR 7464, January 19, 2017). Rather, the ECEL was one possible risk management approach outlined in the rulemaking that proposed to prohibit the use of methylene chloride in most commercial paint and coating removal. This ECEL was not finalized and thus, there is no ECEL for methylene chloride. EPA provided the PEL as a point of comparison only to help readers

	opposed to OSHA's PEL – a very different picture would emerge. For example, under the manufacturing condition of use, the high-end 8-hour TWA exposure concentration (4.6 mg/m3 or 1.32 ppm) would just exceed the ECEL of 1.3 ppm.	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.
Use of limited data sets to extrapolate exposure among broader worker groups		
SACC, 67	**SACC COMMENTS:** • There is concern over the use of limited data sets to extrapolate exposure among broader worker groups. While there is a mathematical approach to identify the central tendency and high-end values when the distribution is unknown, the current data quality assessment does not take into account whether the data are generalizable to the exposures among the entire set of workers that the data are being used to represent. • The risk evaluation does not provide sufficient information on the reasons used by OSHA to collect data at targeted sites, and therefore, the potential for overestimation or bias of general exposures for a specific use is not easily determined. • EPA should include additional information on the basis and purpose of data collection to provide better understanding about why the data reported by OSHA were collected.	EPA states the uncertainty of representativeness as a primary uncertainty for each occupational exposure scenario that includes monitoring data and in the Uncertainties section 4.3.2. EPA added text to Section 2.4.1.1 of the Risk Evaluation and Section 1.4.4.4 of the Supplemental Information on Releases and Occupational Exposure Assessment to add additional information from the OSHA website about why monitoring data were collected.
SACC	**SACC COMMENTS:** • For use categories where EPA analysis determined exposure above the PEL, an additional analysis could be conducted	EPA shows reductions of exposures associated with respirator use in the Risk Characterization. EPA also compares exposures to the OSHA PEL and STEL. EPA does not have an approach of setting the maximum exposure based on data for those companies that are following EPA

	based on the approach of setting the maximum exposure based on data for those companies that are following either OSHA and/or EPA NESHAP regulations. • Evaluate the representativeness of data sets or express the uncertainty in the extrapolated exposures.	NESHAP regulations. EPA has addressed representativeness of data sets and limited data sets in the list of limitations in each subsection of 2.4.1.2 and holistically in the Uncertainties section 4.3.2.1. {Note: This is a repeat response to several similar comments}
Modeling versus monitoring data for occupational exposure estimates		
SACC	**SACC COMMENTS:** • Include a comparison of the exposure model predictions to the monitoring data ("Supplemental Information on Releases and Occupational Exposure Assessment", Section 4.2.3, p. 123) or include an explanation as to why this was not done.	EPA compared monitoring data to model predictions for the one OES, Cold Cleaning (Section 2.7.3 of the Supplemental Information on Releases and Occupational Exposure Assessment), for which both were available. EPA has added explanation to section 2.4.1.2.7 showing this comparison and to explain that monitoring data have higher weight of evidence due to higher relevance than modeling results for this use for several reasons: (1) monitoring data are known to be relevant to this use; and (2) the modeled results cannot be validated and do not capture the full range of possible exposure concentrations identified by the monitoring data for this use.
67, SACC	**SACC COMMENTS:** • The hierarchy of approaches to exposure estimation is not always appropriate. The Agency should develop a protocol for deciding when measurement data of good quality are available in sufficient quantities to derive reliable estimates. If they are not sufficient, modeling could be a preferable approach to available measurements. **PUBLIC COMMENTS:** • When empirical sampling data are outdated or sparse, supplementing such data with modeling would improve the exposure estimates and increase the likelihood that the risk characterization is founded on the best available science.	EPA has included the hierarchy of approaches in Appendix G of the Supplemental Information on Releases and Occupational Exposure Assessment. This appendix shows that 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. EPA used a model and relevant parameter data for one occupational exposure scenario, Cold Cleaning. EPA did not find reasonably available data for modeling of other Occupational Exposure Scenarios (OESs).

MC RESPONSE TO COMMENT

67	**PUBLIC COMMENTS** • EPA provides detailed occupational model descriptions in the draft risk evaluation for MC that appear to be sufficient to reproduce the exposure and MOE estimates (EPA, 2019). However, there are a number of issues regarding the occupational modeling approaches that could be strengthened in the final risk evaluation. • To the degree that modeling has not been completed for MC specifically, existing modeling can be leveraged. Models that have been applied to other volatile organic compounds (VOCs) for well-defined scenarios can be reapplied for MC after adjusting for chemical-specific input parameters (e.g., vapor pressure, usage volumes, etc.). This methodology is consistent with EPA's endorsement of read-across approaches for data gap filling and is appropriate for exposure characterization. • When modelers utilize WOE approaches to develop appropriate input parameters, models may be more appropriate than low-quality monitoring data. • EPA should consider the incorporation of additional modeling in the revised risk evaluation using scenario definitions that are consistent with modern uses and peer review by occupational exposure assessment professionals familiar with current handling practices.	EPA has utilized all modeling opportunities with the reasonably available data, and this includes the use of near-field/ far-field modeling in several well-defined degreasing and brake servicing scenarios. EPA is not aware of other well-defined scenarios that could be reapplied.

41, 45, 66, 67, 68	**PUBLIC COMMENTS:** • EPA's modeling results could be improved by using model inputs that represent more realistic data – such as workplace volumes, weight fraction, and amount used – this is a necessary step. • Available monitoring data can be used for risk modeling inputs rather than using assumptions or defaults. For most uses however, the described empirical data sets are very limited in the number of samples and descriptions of the conditions under which the samples were collected. Because such data should be considered of limited confidence, an alternative evidence integration approach should be considered. In this approach, for each scenario, methods should be informed by the empirical data and models used as a package – not individually in a hierarchy. • Use tiered approaches to exposure modeling to verify model outputs and ensure they represent exposure levels in line with real-world conditions. • A tiered approach to exposure assessment will necessarily outline how EPA chooses which data to include in its analysis and will provide helpful guideposts when choosing between multiple problematic data. • EPA needs to outline a tiered approach towards exposure assessment. In this instance, there are two competing data sets (monitoring data and modeled data) and a cursory justification. A tiered	EPA used reasonable available model input data for modelling occupational exposures in several OESs. EPA considered both monitoring and modeling for the one OES, Cold Cleaning, for which both were available. Monitoring data and thus modeling were not reasonably available for other OESs. EPA does not have tiered approaches or other data necessary to verify any of the occupational models used in this Risk Evaluation.

	approach could provide a scientifically based path forward, and, if needed, suggest further steps such as a Tier 2 exposure model to achieve higher quality data. A tiered approach to exposure assessment would be more consistent with TSCA's Section 26(h) requirement for EPA to rely upon best available science in its risk evaluations.	
EPA should gather additional monitoring data		
SACC	**SACC COMMENTS:** • Include personal monitoring sampling data provided in OSHA (2019) and Finkel (2019) to better characterize MC exposures in a number of occupational exposure scenarios. • While the OSHA (2019) data are used for three exposure scenarios, this data set includes important exposure data that can supplement exposure data used in other scenarios. • Sampling data from the NAICS 325199 code (summarized in Table MC4-1 of the SACC report) should also be incorporated into the occupational inhalation exposure summary metrics presented in Tables 2-28 and 2-29 of worker exposure to MC during manufacturing. • SIC codes provided within Finkel (2019) can be matched with occupational exposure scenarios to provide additional exposure data for a number of scenarios.	• EPA added text to Section 2.4.1.1 of the Risk Evaluation and Section 1.4.4.4 of the Supplemental Information on Releases and Occupational Exposure Assessment to add additional information about OSHA and data provided by Dr. Finkel. • While the values presented in Table MC4-1 are classified as "Manufacturing," these were designated by OSHA and correspond only to NAICS code 325199, which may be applicable to any chemical manufacturing, not specifically MC manufacturing. • EPA added pretreated 8-hr TWA data from Dr. Finkel into the exposure assessment in 11 OESs. The new data added for each OES ranged from 12 to 468 points. The Commercial Aerosol Products OES previously had only modeling but now has monitoring data as well. The Adhesives and Sealants OES has a new Unknown Application Method subcategory (added to Spray and Non-spray categories).
SACC	**SACC COMMENTS:** • State environmental and health agencies can be queried about the availability of	EPA did not find additional reasonably available information for these sources including Washington state, which was contacted. EPA

	monitoring and exposure data relevant to this chemical. These data should be obtained and incorporated into the assessment. Washington State was mentioned as likely having such data that could be shared.	believes that state OSHA data is included in the OSHA Chemical Exposure Health Data set.
49, 72, 73, 75, 76, SACC	**SACC COMMENTS:** • EPA should develop a process to identify critical missing information on uses, PPE, or area and personal monitoring data. • Some of the measurement data available to EPA were not used because critical sample collection information (e.g., duration of sample collection) was not reported by the source of the data. • It is not clear whether EPA exhausted all reasonable means to obtain the missing information; for example, by contacting the authors of a publication or company report, or the laboratory that analyzed the sample. • Indicate clearly whether all proactive venues for obtaining necessary and/or missing information (including uses, PPE, or specific information on monitoring samples) were exhausted and whether indeed there was no way of obtaining these data. • The process of requesting missing information should take place early in the risk evaluation process to allow sufficient time for relevant stakeholders to provide the missing information to fill data gaps and/or strengthen the available information already present. **PUBLIC COMMENTS:**	• EPA added new text about modeling in Section 2.4.1.1 to indicate that beyond the modeling conducted for this Risk Evaluation, EPA did not find reasonably available models and associated parameter sets to do additional modeling. 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. • 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. In general, EPA intends to utilize TSCA data gathering authorities more routinely for the next 20 risk evaluations.

	• EPA has failed to ask employers to share the workplace monitoring data that they are required to preserve under OSHA regulations, or asked OSHA and other state and federal agencies to provide access to the extensive exposure information in their direct possession or made use of the exposure information that is in EPA's possession.	
Selection of sites for collection of occupational exposure monitoring data		
SACC	**SACC COMMENTS:** • It was unclear exactly what EPA meant by "…sites used to collect occupational exposure monitoring data for workers were not selected randomly" (lines 1850-1851) and this appears to be indicating that bias was included in monitoring data. • Provide more context and added justification for how the OSHA monitoring data collected post-1997 are used, describe clearly biases in the OSHA data and any associated uncertainties in the exposure estimates.	EPA revised text in 2.4.1.1 to remove the unclear sentence and to summarize EPA's new statistical analysis, which is included as a new appendix in the Supplemental Information on Releases and Occupational Exposure Assessment. The new analysis has improvements in validity and reliability and uses appropriate statistical methods. In section 4.3.2.1, EPA states the uncertainty of the use of data from before the PEL revision and that use of some older data may overestimate some exposures.
SACC	**SACC COMMENTS:** • Facilities with fewer than 10 employees are not required to report to TRI. • Consider using NPDES data to estimate the number of facilities employing fewer than 10 workers and use these data to assess the potential degree of under-estimation in the current assessment.	• EPA's analysis uses TRI and DMR to estimate the highest local per site water releases of MC and is not intended to estimate overall releases. EPA's analysis uses TRI and DMR to estimate the highest local per site water releases of MC. EPA does not expect that this suggested approach would improve upon EPA's approach or provide higher local per site releases compared to estimates provided using TRI and DMR data. The proposed assumption is that a site that monitors MC discharges per their NPDES permit but does not report to TRI has fewer than 10 full-time equivalent workers. This proposed assumption does not seem reasonable or likely to be valid.
Clarification of calculations for occupational exposure		

MC RESPONSE TO COMMENT

SACC	**SACC COMMENTS:** • The value for Yderm in Table 2-33 is used for the calculations, but the calculated numbers don't match those in the Table 2-57, p. 138. It appears that this is because the value for Yderm should be 0.9 instead of 1.0. The summary table for dermal exposure estimates (Table 2-85, p. 165) shows a value of 0.9 for this worker category. • Reconcile this discrepancy and adjust the text accordingly. • EPA should verify the dermal dose calculations for the commercial, adhesive and caulk removers, and spot cleaning scenarios were performed with Yderm = 0.9.	• EPA corrected Yderm in Table 2-57 for Adhesive and Caulk Removers to be 0.9 instead of 1.0. Values in Table 2-33 are correct and not related to Table 2-57. EPA has verified that the dermal dose calculations for the commercial, adhesive and caulk removers, and spot cleaning scenarios were performed with Yderm = 0.9.
SACC	**SACC COMMENTS:** • Clarify how the minimum, maximum and mean values from the Ukai et al. (1998) study are used to estimate the TWA for calculating the average daily concentration (ADC) and lifetime average daily concentrations (LADC) (Section 2.4.1.2.19, p. 156, lines 3138-3145).	• EPA added clarifying text to both Section 2.4.1.2.19 of the Risk Evaluation and Section 2.19.3.2 of the Supplemental Information on Releases and Occupational Exposure Assessment.
SACC	**SACC COMMENTS:** • Ensure that ADC and LADC estimates are correct and explain discrepancies between estimates derived using Equation 2.5 and estimates derived from the 8-hour TWA measurements. • The Committee was unable to duplicate estimates for ADCs and LADCs presented in Tables 2-39, 2-41, and 2-45 (pp. 122, 124, and 128) using the	• EPA originally calculated ADC and LADC values directly within the Monte Carlo model but revised the Risk Evaluation and the Supplemental Information on Releases and Occupational Exposure Assessment to use Equation 2.5 for consistency with other scenarios.

	approach and equations of Section 2.4.1.1 (p. 107) and the available 8-hour TWA exposure concentrations. These estimates differ enough that they do not appear to be due to rounding in the calculations. • These tables were the only instances where the exposure estimates are from modeling the data rather than calculated directly from monitoring data. If the estimates derived from modeling were handled differently from direct estimates the text should discuss this.	
SACC	**SACC COMMENTS:** • The mean and standard deviation should be included in the parameter distribution tables for the specific lognormal distributions used. Parameters used to define the other distributions are included.	• In the Supplemental Information on Releases and Occupational Exposure Assessment document, the mean and standard deviation for the lognormal distributions are included in the text sections (e.g., Sections F.1.2.3 and F.1.2.11). EPA removed the values in the Lower Bound and Upper Bound columns in Table F-1 for the lognormal distributions (indoor air speed and operating hours per week). EPA included the mean and standard deviation in the Comments column.
Assumptions made in Monte Carlo analysis used in occupational exposure assessment		
SACC	**SACC COMMENTS:** • Expand the discussion on the selection of distributions for the Monte Carlo analysis, particularly for specification of the uniform distributions as the most appropriate choice for an input parameter. • Expand the description and rationale for setting an input parameter to a constant or investigate whether a distribution provides a better description of the exposure range. • It is unclear why the number of spray applications per brake job was set to a constant in the Monte Carlo analysis rather than as a variable with associated	• The specificity of more complex distributions (e.g., triangular, lognormal) requires adequate data to demonstrate the distribution. If only an overall range is known, then a uniform distribution is the only possible distribution to use. There may be some cases where a uniform distribution is appropriate if data indicate it as such. But generally, for EPA's modeling, uniform distributions were used because no data were found to demonstrate a more sophisticated distribution. EPA added text in Appendix F.1.2 of the Supplemental Information on Releases and Occupational Exposure Assessment for clarification. • EPA defined distributions for model parameters where EPA had data or information to justify the distribution. Model parameters kept as constants were generally cases where EPA did not have reasonably available data to describe the variability or uncertainty of the parameter value (e.g., number of brake jobs per site-year, number of

	distribution. The comment in Table Apx F-1 of the risk evaluation for number of applications per job (NA) is uninformative	ounces of aerosol degreaser used per job). Some model parameters were kept as constants by choice (i.e., temperature and pressure are constant as the model is isothermal and isobaric) and some were kept as constants appropriately (i.e., the molecular weight of MC is appropriately kept constant). EPA added text in Appendix F.1.2 of the Supplemental Information on Releases and Occupational Exposure Assessment for clarification.
Recommending alternative occupational risk approaches		
SACC	**SACC COMMENTS:** • One Committee member suggested a Monte Carlo approach to ensure that variability and uncertainty are handled within one consistent framework. • It was suggested that EPA use a probabilistic approach in the risk calculation derivation by providing each parameter (including fate properties, amount of MC discharged directly or indirectly in water sources, number of facilities that use or discharge MC, frequency of release, assigned protection factor (APF), extent of use of PPE, and UF used) with distributions derived from previous studies, rather than using a mixed approach where certain parameters are kept fixed, while others are sampled from uniform distributions with ranges derived from the literature. • By using a Monte Carlo approach, it would be easier to make probability statements regarding both optimistic and pessimistic projections, which the Committee member believed were hard to quantify directly from the risk evaluation.	EPA incorporated probabilistic modeling in several analyses in the Risk Evaluation. EPA conducted probabilistic assessments for occupational exposure using the Near-Field / Far-field model when parameter values were reasonably available. Deterministic assessments were only used when lack of parameter distributions prevented probabilistic assessments. For the human health hazard, EPA also used probabilistic models (Monte Carlo analyses) for the dose-response models for chronic non-cancer and cancer endpoints.

Recommending alternative occupational exposure assumptions		
SACC	**SACC COMMENTS:** • For chronic exposure, extended working years should be factored into the assessment, since workers continue to work past the traditional retirement age, including ages 65-74 and 75 and older. • Information on employed persons, by occupation and industry and age, is provided by the U.S. BLS and can be used to inform industry specific working age for chronic exposure calculations (BLS, 2019).	• EPA used BLS data to develop a distribution of working years. The max of the distribution is 44 years and the calculated 95th percentile is 40 years. The distribution included low tenure to reflect workers who change industries. Appendix C of the Supplemental Information on Releases and Occupational Exposure Assessment contains a more detailed explanation on how the distribution was derived.
66	**PUBLIC COMMENTS:** • EPA was not clear about which age groups were included in the occupational exposure assessment; inhalation exposure was not presented by age group. • EPA should indicate when reproductive age ends for men. • The health effects of women >50 years of age, and the elderly was not considered, this is not health protective and does not take into account that this population is vulnerable (p. 105). • Line 6823: Calculate adults but define them as >16 years of age. Also, calculate 40 years working when the retirement age (16+40 years) would be 56 years. • p. 300: Include 16-year-olds because they are able to obtain permits, even though most workers are adults.	• At the beginning of section 2.4.1, EPA states that for the purpose of this assessment, EPA considered occupational exposure of the total workforce of exposed users and non-users, which include but are not limited to male and female workers of reproductive age who are >16 years of age. Female workers of reproductive age are >16 to less than 50 years old. Adolescents (>16 to <21 years old) are a small part of this total workforce. The occupational exposure assessment is applicable to and covers the entire workforce who are exposed to MC. • There was no upper limit on male reproductive age assumed for this evaluation.
72, SACC	**SACC COMMENTS:** • For high-end acute exposure scenarios, the risk evaluation should incorporate longer shift lengths (exposure periods)	• EPA added the 12- hr shift data from HSIA for the Manufacturing OES and updated the corresponding equation defaults in Section 2.4.1.1 of the Risk Evaluation and Appendix C of the Supplemental Information on Releases and Occupational Exposure Assessment, as

	informed with data from the HSIA surveys (up to 12 hours). • This is relevant to each exposure scenario as well as to the calculation of the acute exposure concentration (equations 2-4 and 2-5) as it relates to exposure duration, and averaging time. • The U.S. BLS provides industry-specific data on weekly hours worked, which, on average, are beyond 40 hours for the manufacturing industry (BLS, 2019). **PUBLIC COMMENTS:** • EPA should clarify whether its 8-hour TWA values for manufacturing account for the longer work shifts indicated by HSIA, and, if not, should revise its calculations to reflect those workers' increased exposures, as well as those for any other workers who work shifts longer than 8 hours.	HSIA indicated that 12-hr shifts were also common. 12-hr data are presented separately and no changes were made to the 8-hour shift data.
Uncertainty and recommended probabilistic assessment		
SACC	**SACC COMMENTS:** • The potential for introducing bias when classifying uses and type of worker activities into these categories is not transparent. If the exposure estimate is based on reported measurement data, and those data are for one or very few worker activities within the user/occupational exposure scenario (OES) category, it could potentially underestimate or overestimate exposures for other worker activities included in the same OES. • A more detailed description of this potential bias is needed.	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*. EPA describes the data integration approach and factors considered in determining levels of confidence for the occupational 8- or 12-hr TWA data and estimates and dermal potential dose estimates in an appendix added to the Supplemental Information on Releases and Occupational Exposure Assessment.

	• While EPA describes the sources of uncertainty in exposure estimates (including PPE), it is not clear how these uncertainties translate into data quality and overall confidence designations. • Describe in a transparent manner how EPA derives data quality ratings and overall confidence levels, so it is clear how uncertainties are reflected into these evaluations	
66	**PUBLIC COMMENTS:** • EPA should consider conducting a probabilistic risk assessment for exposure data. The EPA considered the central tendency and high-end exposures to conduct deterministic risk assessments for the different exposure scenarios. When performing a deterministic analysis, only one value is inserted per parameter, which results in a single point estimate. However, single point estimates may not provide an accurate or realistic depiction of the exposure scenario, and less is understood about variability and uncertainty.	EPA conducted probabilistic assessments using the Near-Field / Far-field model when parameter values were reasonably available. Deterministic assessments were only used when lack of parameter distributions prevented probabilistic assessments.
Consumer exposure assumptions		
SACC	**SACC COMMENTS:** • The Agency does not consider that there is an increasing number of people that engage in activities using products, such as adhesives, more frequently and for longer periods than the typical occasional user. • EPA should recognize that a sector of the population could be at increased risk from exposure than the typical consumer	The uncertainties associated with the use of USEPA (1987) are discussed in Section 4.3.3. A sentence has been added to explain that an increasing trend in do-it-yourself type activities may lead to an underestimate in exposures. Nevertheless. the range of use patterns evaluated (10^{th} to 95^{th} percentile) is expected to cover the reasonable range of possible exposures.

	because they engage in hobby-type activities for both pleasure and profit. Essentially, they could be considered home-based workers. • The Agency should consider developing methods for assessing the size and risk from exposure for this subpopulation.	
SACC	**SACC COMMENTS:** • Clearly define the brush cleaner condition of use in the risk evaluation. • This is a condition of use that was not considered in the 2014 risk evaluation, which has much lower use percentages and differing use patterns when compared to paint removers/strippers into which EPA categorizes this product. • This is significant since it was the only consumer condition of use that met the "does not present an unreasonable risk" criteria.	As noted by the commenter, brush cleaning products contain methylene chloride in lower concentrations than paint removal products and were not included in the 2014 risk assessment. In the case of methylene chloride, EPA considers use as a brush cleaner to be distinct from use in paint and coating removal more broadly, as reflected by its inclusion in the risk evaluation. Due to the potential for brush cleaning to have impeded dermal evaporation from dermal immersion, this condition of use was re-evaluated using the CEM Permeability submodel in our revised dermal evaluation. In the revised evaluation, risk was identified, resulting in a determination of unreasonable risk in the final evaluation.
SACC	**SACC COMMENTS:** • One Committee member mentioned that while MC is a solvent that may be used in some children's product manufacturing processes (e.g., metal component degreasing, solvent bonding, paint/ink carriers), due to its high volatility, significant concentrations are unlikely to remain in products as received by consumers. • Some manufacturers are reporting this substance under state reporting statutes at concentrations of up to 10,000 ppm. • The informed Committee member considered reported concentrations this high are very unlikely to be accurate, and	EPA appreciated these comments as they give context to possible MC concentrations in consumer products. All consumer products were evaluated based on current conditions of use and known consumer product properties as reported on their SDSs. No known products that were expected to be used by children specifically were identified .

	instead reflect over-reporting, which is common.	
SACC	**SACC COMMENTS:** • One Committee member noted that a comprehensive accounting of MC in consumer products may be obtained from the California Air Resources Board which collects this information, including weight-percent and estimated emissions. • A summary of these data was provided to EPA for the docket.	EPA appreciates the potential source of information. EPA is aware and uses CARB as a data source in developing the COUs for chemicals and to help ensure the COUs analyzed in the Risk Evaluation is comprehensive. In practice, for products, the Agency prefers to cite information directly from the company (often in the form of SDS) to ensure it is the most current formulation and the product is still available in the marketplace.
SACC	**SACC COMMENTS:** • Pratt et al. (2005) reported method detection limits for MC that are representative for the studies by Adgate et al. (2004) and Sexton et al. (2007) because measurements were made with the same sampler and sampling/analysis protocol, and the analysis was performed by the same laboratory in all these studies. • These values could be reported in Tables 2-120 and 2-121 (pp. 194-195) with an appropriate footnote. • Table 2-121 appears to reference the Adgate et al. (2004) study twice as the corresponding text refers to only two studies and the Adgate et al. (2004) study rows only differ by the Detection Frequency (DFq) values.	EPA appreciates these citations as relevant sources of information. Adgate et al. (2004) was re-reviewed for mention of detection limits (DL) and while the article does not include quantitative DLs it does include mention of an article that better describes the methodology used in the study. That study (Chung et al. (1999)) was reviewed and found to have representative DLs. A footnote has been added to tables where Adgate is discussed citing the relevance of the DL found within Chung et al. (1999)
73, 75	**PUBLIC COMMENTS:** • It is not realistic to assume that consumers are only exposed once to consumer products containing this substance in view of how these products are used.	Scenarios for conditions of use associated with products containing MC 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

	• The MC problem formulation commits EPA to evaluate risks to "subsets of consumers who may use commercially-available products or those who may use products more frequently than typical consumers" (p. 65), however the draft evaluation does not follow through on this commitment. • EPA's final evaluation must address chronic cancer risks to consumers based on scenarios of recurring and/or multiple consumer product use. • EPA's assumption about consumer exposure seems likely to significantly underestimate the risks they face. EPA needs to conduct a sensitivity analysis regarding these assumptions in the risk evaluation, which is different than the sensitivity analysis that EPA indicates was done on the model itself (p. 179).	also following use through the prescribed movement about the house. 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 US EPA (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. Although high-end frequencies of consumer use are up to 50 times per year, reasonably available toxicological data is based on either single or continuous MC exposure and it is unknown whether these use patterns are expected to be clustered or intermittent (e.g. one time per week). There is uncertainty regarding the extrapolation from continuous studies in animals to the case of repeated, intermittent human exposures. Therefore, EPA cannot fully rule out that consumers at the high-end frequency of use could possibly be at risk for chronic hazard effects, however it is expected to be unlikely. Bystanders exposures would be expected to be appreciably lower than user scenarios. This uncertainty on frequency of use patterns is mentioned within Section 4.3.3 as an uncertainty within the consumer exposure evaluation and notes that the possibility of more DIY-type consumer users may underestimate exposure, but that US EPA (1987) is the currently the most up-to-date, nationally comprehensive resource available for evaluating consumer use patterns. • The evaluation of subsets of consumers that may be high-end users is addressed in Section 4.4.3. The uncertainties and assumptions have been edited to better describe uncertainties associated with high use consumer like hobbyist and do-it-yourself consumers by adding, "…consumer movement towards more do-it-yourself projects with products containing the chemical may lead to an underestimate of consumer use patterns described within the survey in some instances. Nevertheless EPA assumes that the use pattern data presented in U.S. EPA (1987) reflects reasonable estimates for current use patterns of similar product type. These estimates were deemed to be reasonable

		due to the range of use patterns evaluated (e.g., ranging from 10th to 95th percentile) and that this dataset represents the most recent, relevant and nationally-representative data available for use pattern data in most cases." • The assumptions and uncertainties associated with our consumer exposure evaluation is fully described in Section 4.4.3. A description of the sensitivity analysis on the overall CEM model is described in Section 2.4.2.3.3 and Appendix G. It is unclear as to which assumptions about consumer exposure the commenter is referring to that would lead to an underestimate in risk, but 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.
73, SACC	**SACC COMMENTS:** • EPA should consider carefully the assumption that the bystander(s) will remain in a different room (Zone 2 for modeling) during use of a product. Depending on the actual use, product, and specific application, the assumption of far-field location for the bystander(s) during use may not be sufficiently conservative. • Reconsider whether bystanders are always located in a different zone than the user for the consumer use scenarios, independent of the type of product. • At a minimum, EPA should specifically address the uncertainty about bystander location depending on specific product use.	As explained in Section 2.4.2.3.1, EPA states that the bystander was assumed to remain outside the room of use as a bystander entering the room of use would be expected to approximate the exposures associate with a user. As a way to better communicate this assumption it has been added to the Assumptions and Uncertainties for Consumer Exposure Section (Section 4.3.3) It has been clarified in Section 2.4.2.3.1 that a user or bystander may enter/re-enter the room of use depending on the modeled room of use and prescribed activity patterns.

73	**PUBLIC COMMENTS:** • EPA recognizes that "[r]esidential bystanders for consumer uses are expected to be indirectly exposed to methylene chloride and may be of any age" (p. 275), but the Agency does not appear to have actually assessed exposure to all age groups. • EPA provides no rationale for excluding infants and children under the age of 3 years in its evaluation. Infants, relative to older children and adults, have a higher breathing rate per unit body weight and, as acknowledged by EPA, may be particularly susceptible to the neurotoxic effects of MC due to their higher residual levels of fetal hemoglobin that has a higher affinity for carbon monoxide (CO) (p. 32).	As described in Section 2.4.2.3.2, dermal exposure results are presented for users of three possible age groups: adults and two youth age groups (16-20 years and 11-15 years). Inhalation exposures are presented as concentrations encountered for users and non-user bystander populations and are independent of age group. In developing the hazard assessment, EPA described human subpopulations that may have greater susceptibility than the general population to hazards of MC (Section 4.4). As described in Section 3.2.5 (Dose-Response Modeling), EPA used PBPK models for toxicokinetic differences (for chronic risk) and intraspecies UFs in the risk evaluation. The intraspecies UF was established to account for uncertainty and variability that includes susceptible subpopulations (EPA, 2002). Research indicates that a factor of 10 (when including both toxicokinetics and toxicodynamics) is sufficient in most cases (EPA, 2002).
77	**PUBLIC COMMENTS:** • Bystanders may experience elevated inhalational exposures if they live or work adjacent to a workplace where MC-containing products are used. EPA assumes that bystander inhalation exposures would be acute, these exposures can, in fact, be chronic. • Chronic bystander exposures should be systematically studied and appropriately addressed by EPA under TSCA. • This is especially important given EPA's conclusion that "[c]onsumer and bystander inhalation exposure . . . is expected to be the most significant route of [consumer] exposure through the	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 US EPA (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. Although high-end frequencies of consumer use are up to 50 times per year, reasonably available toxicological data is based on either single or continuous MC exposure and it is unknown whether these use patterns are expected to be clustered or intermittent (e.g. one time per week). There is uncertainty regarding the extrapolation from continuous studies in animals to the case of repeated, intermittent human exposures. Therefore, EPA cannot fully rule out that consumers at the high-end frequency of use could possibly be at risk for chronic hazard effects, however it is expected to be unlikely. Bystanders exposures would be expected to be appreciably lower than

	direct inhalation of sprays, vapors, and mists."	user scenarios due to greater distance from and less time spent in the room of use. This uncertainty on frequency of use patterns is mentioned within Section 4.3.3 as an uncertainty within the consumer exposure evaluation and notes that the possibility of more DIY-type consumer users may underestimate exposure, but that US EPA (1987) is the currently the most up-to-date, nationally comprehensive resource available for evaluating consumer use patterns.
66	**PUBLIC COMMENTS:** • The consumer exposure modeling parameters shown in Table 2-87 indicates a background MC concentration of 0 mg/m^3. However, from Table 2-121, the baseline concentration is not 0.	Consumer modeling for specific condition of use scenarios was modeled with a background concentration of zero since documented concentrations referenced in Table 2-121 could not be tied to a specific condition of use. This uncertainty has been added to Section 4.3.3
41, 68, SACC	**SACC COMMENTS:** • Section 3.2.5.2 states "A 1-hour value is used for consumer settings, which is similar to the length of time (1.5 hours) after which effects were observed by Putz et al., (1979)." • One hour seems too short to estimate consumer exposures, even just based on the few fatality case studies described in Appendix J. • In estimating consumer exposure for specific uses, different time lengths were used; hence, the risk evaluation does not rely exclusively on the 1-hour assumption. • The exposure time for consumer exposures for all uses (scenarios) should be detailed in Section 3.2.5.2 or in an associated appendix/supplemental file. **PUBLIC COMMENTS:** • EPA should ensure that duration and product amounts within the conditions of use represent realistic values. In modeling	As described in Section 2.4.2.3.1, exposure inhalation consumer durations are presented as maximum 1-hour and 8-hour TWAs over the course of the 72-hour model run. Most of the timing related to deaths is not known but one occurred within 2 hours 20 minutes, as stated in Appendix J of the risk evaluation. The effect being used in the risk evaluation occurred after 1.5 hours of exposure. The data used from Westat represent the most current, nationally relevant data source available for a range of the evaluated conditions of use. Westat was used principally as support for the length of time a product was used 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. All weight fractions used in this evaluation are derived from SDSs for products that are available to or marketed to consumer users. EPA notes there are limitations and uncertainties associated with this Westat dataset. Those limitations and uncertainties are discussed fully in Section 2.4.2.6 With regard to clarity in concentrations assumed by EPA the evaluated weight fractions associated with products of a particular condition of use are available in Table 2-90. In addition, estimated dermal and inhalation exposure concentrations, are found in Section 2.4.2.4

	consumer exposures, for example, EPA estimated the duration and product amount corresponding to the 10th, 50th, and 95th percentile values based on data from the 1987 EPA publication, Household Solvent Products: A National Usage Survey. Certain durations, however, seem excessive for consumer exposures. • Likewise, certain mass of product use assumptions for consumer exposures seem excessive. EPA should develop and/or use more current and/or relevant exposure scenarios/data to estimate the duration of use and amount of use of consumer products containing MC. • EPA used historic data (WESTAT, 1987) for information regarding duration of use and quantity of use. In some cases, the scenarios do not seem plausible. They have assumed that consumers use high-concentration, industrial products, that are not intended for consumer use. • EPA should consider the validity of certain exposure scenario data and the relevance of historic data used to describe current consumer exposure scenarios. • The concentrations that EPA is assuming are not clear. This information is not discussed specifically for the individual products. • EPA's exposure values for consumer use scenarios include peak concentrations that appear to overpredict levels, including levels are in excess of 7000 mg/m^3, a level that is immediately	The reported consumer exposure evaluations are anticipated to cover a plausible range of possible exposure conditions ranging from a low-intensity to a high-intensity user. The referenced scenario where this value occurs represents a condition of use where the evaluated product has a weight fraction of 100% MC, thereby providing support for the estimated high value.

	dangerous to life or health according to NIOSH.	
Use and market profile		
SACC	**SACC COMMENTS:** • In the Use and Market Profile for Methylene Chloride (EPA 2017), reconfirm product links and update profiles, eliminating products that no longer contain MC.	The Use and Market Profile contributed to the basis of EPA's identification of the conditions use for the purposes of the scope and problem formulation documents for methylene chloride. The document presented publicly available information as of the date of the document on the manufacturing (including importing), processing, distribution in commerce, use, and disposal of methylene chloride and was used to inform decisions regarding conditions of use. The document does not reflect information received directly from other sources such as manufacturers, processors, etc., which has further informed EPA's understanding of the conditions of use. As such, the uses and products identified in the document may differ from EPA's current understanding. If any of the products are associated with conditions of use determined to have unreasonable risk, EPA will reconfirm product links and profiles during the risk management process.
Consumer exposure model		
SACC	**SACC COMMENTS:** • The potential exposures of the general public to MC need to be clarified further and/or expanded. • The CEM assumes zero baseline concentration of MC. Despite not considering aggregate exposures, EPA should indicate that this assumption is not conservative; population exposure data show that there are measurable concentrations of MC in the indoor air of homes as well as in the personal breathing zone of the occupants. • On the other hand, blood concentrations of MC were undetectable in 2,878 individuals measured as part of the 2009-2010 National Health and Nutrition Examination Survey (NHANES). These	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, for which long-standing regulatory and analytical processes already exist. Because stationary source releases of methylene chloride to ambient air are adequately assessed and any risks 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 methylene chloride is currently addressed in the SDWA regulatory analytical process for public water systems, EPA did not include this pathway in the risk evaluation for methylene chloride under TSCA. In Problem Formulation, EPA also found general population exposures to methylene chloride 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

	findings are not discussed in detail in the risk evaluation and these observations should be better explained.	jurisdiction of and addressed by other EPA-administered statutes and associated regulatory programs. 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.
SACC	**SACC COMMENTS:** • The rationale for setting the modeling inputs for the weight fraction (Section 2.4.2.3, p. 168, lines 3449-3452) is unclear. • Explain why only the maximum and minimum were used to determine modeling inputs if the weight fraction was <40% but the maximum, minimum, and midpoint were used if the weight fraction was >40%.	Weight fractions were derived from product specific SDSs. Depending on the product information and number of found products, those weight fractions could end up encompassing a range of possible weight fractions. The midpoint weight fraction was evaluated for ranges >40% to better evaluate the range of possible exposures. Language has been added to this section to clarify these points.
SACC	**SACC COMMENTS:** • Further justification is required for current approaches used to characterize consumer dermal exposure. • There is concern that the dermal surface area for exposure indicated in Table 2-88 seems low – 10% for activities that involve spray and inside of both hands for some of the cleaning surveys. o The only justification of this assumption is provided in footnote 6, p. 176 of the risk evaluation, which indicates "Selected dermal SA/BW ratio used is based on CEM scenario used or best professional judgment for Generic Scenario." The justification would be strengthened by including additional supporting information, not limited to an indicator of which scenarios use dermal surface area	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 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 2.4.2.3. Included in that re-evaluation is description and revision to the SA/BW ratios used in EPA's evaluation. For those evaluations using the Permeability approach, EPA used either full hand or both hands SA/BW ratios since those conditions could involve wiping with a chemical soaked rag that would be expected to cover the whole hand. Meanwhile, those offering unimpeded dermal exposure tended towards continued use of the 10% of hands SA/BW ratios. Those selected SA/BW ratios are identified in Table 2-90.

	based on the CEM scenario and which are based on professional judgment. The justification should also discuss if the dermal surface area of exposure assumptions include dermal exposure from the product application as well as dermal exposures through rags containing product or spills on clothing, which likely occur in these consumer scenarios and which could increase the dermal surface area to which consumers are exposed. • The Committee recommends that EPA document the dermal surface area assumed for each occupational condition of use exposure scenario indicate which estimate is based on CEM and which is based on best professional judgment and indicate whether the dermal exposure estimate includes application exposures, rag exposures, and spills to clothing.	
45, 66	**PUBLIC COMMENTS:** • The consumer assessments utilized EPA's CEM (relied merely on CEM, without real simulation data). There was high confidence in this model, without supporting justification for its use. EPA should justify the CEM and perhaps benchmark its results with another model.	CEM was used for the evaluation of both dermal and inhalation consumer exposures. As outlined in Section 2.4.2.3.1, there are several reasons for the selection, use, and confidence in this model including aspects such as it has undergone peer review. Thus, there was high confidence in the selection of this model. Particular confidence in the results of this model ranged from low to high depending on the route and available information informing parameterization which is discussed in Section 2.4.2.6. There was no other model suggested that could be used to benchmark these results.
68	**PUBLIC COMMENTS:** • EPA indicated that it has run sensitivity models for the CEM, EPA did not supply elasticity values for specific inputs. This information would help EPA focus data collection efforts on inputs that have greater impact on the model results.	As described in Section 2.4.2.3.3, 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. 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.
68	**PUBLIC COMMENTS:** • Data that EPA incorporates as input values into consumer models must undergo a review to determine whether they reasonably depict real world conditions. EPA should implement a quality review system for SDSs it might consider in TSCA risk evaluations, removing SDSs and associated weight fraction values that do not represent real world conditions. Improper input values can lead to grossly overestimated exposure levels, as is the case with the coil cleaner condition of use.	Input values for modeling purposes uses actual product or scenario values wherever possible to represent use scenarios as accurately as possible. The evaluated weight fraction for the coil cleaner scenario was a value given within the specific product SDS (60-100%). Since the value is given as a range, EPA evaluated the product as if it could be both at the low and high end of that range to cover the range of possible exposures. It was assumed the given industry was reporting their product accurately so there is no evidence it does not represent a real world condition or would result in an overestimation in exposure.
General population exposure		
SACC	**SACC COMMENTS:** • The data provided by EPA is incomplete and suggest EPA is in possession of other data. As part of the Total Exposure Assessment Methodology (TEAM) studies, EPA measured concentrations of MC in residential indoor and exhaled breath (Wallace et al., 1991) before the lowering of the PEL. • The Agency and the Health Effects Institute (HEI, Boston, MA) also sponsored the Relationship between Indoor, Outdoor, and Personal Air (RIOPA) study (Weisel et al., 2005a, b, c). • Phillips et al. (2005) also monitored indoor and personal air for selected VOCs, including MC, in four Oklahoma	EPA reviewed the suggested references. In the case of Phillips et al. (2005) and Weisel et al (2005a), the studies were reviewed and not found to have any extractable quantitative information for MC. Wallace et al. (1991) was reviewed and received a medium quality rating. Extracted information was added to Table 2-120. Measured indoor concentrations in this study were in the range of other reported values within Table 2-120 of the Risk Evaluation.

	cities.	
Occupational short-term sample duration ranges		
SACC	**SACC COMMENTS:** • It is unclear why the 15- and 30-minute samples (Section 2.4.1.2.1, p. 115, Table 2-29) are categorized using the bounds of 15-29 and 30-59 minutes, respectively, given that, for instance, a 29-minute exposure is closer to a 30-minute sample than a 15-minute sample. • EPA must justify the time ranges used or adjust ranges of 15-22.5 minutes and 22.5-45 minutes for the 15- and 30-minute samples, respectively.	EPA globally adjusted short-term groupings as recommended and to be consistent included the short-term groupings in Section 2.4.1.2.1 of the Risk Evaluation and in Section 2.1.3 of the Supplemental Information on Releases and Occupational Exposure Assessment.
Dermal exposure assessment		
SACC	**SACC COMMENTS:** • Include a discussion of uncertainty related to dermal exposure assessment in Section 4.3.7 of the risk evaluation.	A discussion of uncertainty related to dermal exposure assessment was added to Section 4.3.7 of the risk evaluation.
45, 73	**PUBLIC COMMENTS:** • The dermal exposure assessment appears to be based on the maximum default quantity that can remain on the skin, rather than actual measurements. • Given the chemical properties (e.g., volatility) and industry uses of MC, this methodology is not justified. Empirical data are available that might inform better absorption estimates and should be considered. EPA should provide additional justification for such assumptions and consider modeling tools for better estimations.	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 MC, 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 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.
41, 49	**PUBLIC COMMENTS:** • EPA's approach to dermal exposure modeling for MC includes fraction	For consumer dermal exposure modeling, the assessment has been revised to incorporate both fraction absorbed and permeability based approaches

	absorbed models for both consumer and occupational exposures. This contrasts with prior draft risk evaluations that have used permeation models for consumer exposures. EPA acknowledges that "fractional absorption may vary and is dependent on various factors ..." EPA's should further justify use of this approach.	dependent on how the particular COU is expected to be used. That revised approach is discussed in Section 2.4.2.3.
63	**PUBLIC COMMENTS:** • Significant dermal absorption, even with the use of gloves, is expected for many of the occupational exposure scenarios listed in Table 4-104. Dermal absorption should be accounted for in a cumulative risk assessment of all exposure routes. This would be useful to the risk management phase by identifying dermal exposures that cause the risk estimate to exceed the MOE.	Regarding cumulative risk assessment by all routes, 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. .
72, 73, SACC	**SACC COMMENTS:** • Exposure modeling in the risk evaluation assumes dermal exposure limited to one event/day – even in the high-end exposure scenario. This assumption may underestimate potential exposures. EPA should provide a more thorough explanation of why the assumption of a single dermal exposure per day was used. EPA should also consider the possibility of more than one exposure per day per worker since workers are likely to encounter the chemical throughout their workday. Multiple exposure events are even more likely in high-end exposure scenarios.	EPA has described events per day (FT) as a primary uncertainty for dermal modeling in the discussion of occupational dermal Uncertainties section 4.4.2.3. This discussion also notes that this assumption likely underestimates exposure as workers often come into repeat contact with the chemical throughout their workday.

	PUBLIC COMMENTS: • EPA acknowledges that this assumption "likely underestimates exposure as workers often come into repeat contact with the chemical throughout their work-day," but did not account for this underestimation or provide any sort of uncertainty analysis. • EPA would need to have robust data demonstrating only a single exposure event occurs per day before incorporating such an assumption into its models. EPA has not provided any such data.	
68	**PUBLIC COMMENTS:** • EPA must implement a tiered dermal modeling approach to ensure the dermal values considered in the assessment accurately reflect occupational conditions. Modeling programs such as IHSkinPerm can produce needed detail during the exposure assessment process and ACC encourages EPA to incorporate this model into future assessments.	EPA has not found reasonably available data and models to conduct tiered modeling for occupational dermal exposures to MC. IHSkinPerm does not have necessary parameters for the uses of MC and requires the user to input parameters (e.g., deposition rates and frequencies) for which EPA does not have reasonably available data.
49, 73	**PUBLIC COMMENTS:** • EPA indicates that it "considered potential dermal exposure in cases where exposure is occluded," referencing the Supplemental Information on Releases and Occupational Exposure Assessment document (p. 111). That document found exposures that are 8-37 times higher than the no-glove scenarios. These exposure scenarios were not incorporated into the risk characterizations. • For example, when comparing Table 2-85 in the draft risk evaluation (p. 165) to	See further discussion on occlusion in Appendix E 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.

	Table 3-3 in the Supplemental Information on Releases and Occupational Exposure Assessment document (pp. 118-119), they present identical exposure estimates with the exception that all of the columns for occluded exposures have been removed from Table 2-85.	
Default surface area values used for modeling dermal occupational exposures		
73, SACC	**SACC COMMENTS:** • EPA should indicate why an upper bound for hand surface area was not used. The Agency should indicate how the dermal exposure and risk evaluation would have changed had they decided to use an upper percentile value for hand surface instead of the average. • Expand the discussion of hand surface area to more adequately describe the exposed surface and include dermal exposure to forearm to better describe the high-end exposure scenarios. The Agency clarified at the face to face meeting, that this area likely represented more than just hand surface. **PUBLIC COMMENTS:** • The two-hand assumption may underestimate exposure because other areas of the body may be exposed to the chemical either through splashes or via deposition of vapor.	EPA has clarified in section 2.4.1.1 regarding the assumption of contact surface area of 1,070 cm^2 as an input parameter for estimating high-end dermal exposure to liquids. This clarification includes that value is equivalent to the 50^{th} percentile surface area of two-hands for males, the highest exposed population. The clarification also includes discussion that EPA has no reasonably available information on actual surface area of contact with liquid and that the value is assumed to represent an adequate proxy for a high-end surface area of contact with liquid that may sometimes include exposures to much of the hands and also beyond the hands, such as wrists, forearms, neck, or other parts of the body, for some scenarios.
Consideration of vapor exposure in dermal occupational exposure estimates		
73, SACC	**SACC COMMENTS:** • Discuss the potential of the vapor to the skin exposure route, including penetration of the vapor through clothing	An analysis in Section 2.5.1 of the Problem Formulation of the Risk Evaluation for MC shows that absorption of MC 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 MC. EPA included

	fabrics, and incorporate it in the dermal exposure estimates if suitable data are available to estimate the contributions to exposures. This pathway should be mentioned for occupational users and ONUs, and EPA should indicate why it was not considered. • EPA should contact ASTM-International and the NFPA about test data for penetration of MC vapor and revise the sources of dermal exposure appropriately, if needed. • The assumption that volatilization is accounted for in the estimates of dermal exposure to occupational users needs further clarification/justification.	expanded discussion in 2.4.1.1 about the f_{abs} parameter that accounts for volatilization in the estimates of dermal exposure to occupational users.
Need to aggregate exposure across inhalation and dermal pathways		
SACC 43, 54, 57, 66, 72, 73, 75, 77	**SACC COMMENTS:** • The committee discussed the need to aggregate exposures through multiple routes and perform a risk evaluation on overall exposure, not only components through specific route and the need to assess and indicate whether one route of exposure is clearly more important than another in order to prioritize mitigation approaches. **PUBLIC COMMENTS:** • Because both inhalation and dermal exposure result in systemic distribution of MC, it is essential to evaluate exposures from both of these routes in combination, including simultaneously, to assess total body burden and the associated effects. • The rationale that the dominant exposure pathway is inhalation due to MC's	MC has a PBPK model for inhalation but not dermal exposure. EPA chose to assess the inhalation pathway for human health, as it is the driver of risk for human health. EPA has added language to uncertainties section explaining how this could lead to an underestimation of risk, as dermal exposure was not incorporated into that analysis. 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 best available science to determine whether to consider aggregate or sentinel exposures for a particular chemical. EPA has determined that using the

	physical-chemical properties is insufficient, given that EPA found significant risk from dermal exposure alone for many conditions of use, including for some where it assumed use of gloves with a protection factor (PF) 5 or 10 (pp. 344-349). • Combining dermal and inhalation exposure would clearly provide a more realistic picture of actual risk.	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.
Uncertainty is not rationale for failing to aggregate inhalation and dermal		
43, 44, 49, 63, 72, 73, 75	**PUBLIC COMMENTS**: • EPA states that it "chose not to employ simply additivity of exposure [routes] at this time … because of the uncertainties present in the current exposure estimation procedures." • The "uncertainties" were associated with its physiologically based pharmacokinetic (PBPK) model that lacks a dermal compartment and therefore "a PBPK model for aggregating inhalation and dermal exposures is not reasonably available." • It is not clear what "uncertainties" EPA is referring to. In fact, EPA derived dermal PODs by extrapolation from inhalation PODs, using toxicokinetic information to	MC has a PBPK model for inhalation but not dermal exposure. EPA chose to assess the inhalation pathway for human health, as it is the driver of risk for human health. EPA has added language to uncertainties section explaining how this could lead to an underestimation of risk, as dermal exposure was not incorporated into that analysis. 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 best

	estimate dermal doses at which the effects seen in inhalation studies would occur. Since EPA had sufficient confidence in route-to-route extrapolation to base estimates of dermal risk on the results of inhalation studies, it is hard to understand why this same approach could not be used to determine overall exposure by the two routes combined. • These uncertainties do not provide a basis for ignoring realistic exposure scenarios.	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.
Failure to aggregate exposure pathways leads to underestimate of risks		
44, 72, 75, 77, 66, 43, 57	• Although the draft evaluation demonstrates that MC presents serious and unreasonable risks to health, its risk determinations examine individual sources of exposure in isolation and fail to estimate the overall risks to consumers and workers from these exposure sources combined. • Aggregation of multiple pathways that contribute to individual exposure would result in even smaller MOEs for acute and non-cancer chronic effects and larger carcinogenicity risks under MC's conditions of use. The lack of aggregation may also lead the declaration of "no unreasonable risk" when one actually exists. • By failing to analyze aggregate exposures, EPA underestimates the health hazards posed by MC. Even if there are uncertainties inherent in the estimation of aggregate exposures, EPA should consider aggregate exposures and, if	• 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 science. EPA has added language to the Key Assumptions and Uncertainties section describing these assumptions and uncertainties. • 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

	needed, append a discussion of the associated uncertainties or potential for estimation errors.	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. • EPA did not consider background exposure that workers and consumers using products containing MC might be exposed to in addition to exposures from TSCA-regulated conditions of use. This may result in an underestimation of risk, and additional discussion of this underestimation has been added to the document in the Key Assumptions and Uncertainties section.
49, 73, 42, 70, 75, 69, 72	**PUBLIC COMMENTS:** • EPA draft risk evaluations have assessed worker exposure in isolation from other pathways and this approach understates risks. EPA should combine exposures from all relevant pathways and determine an aggregate risk reflecting the contribution of each source. This is a further reason why setting a higher cancer risk threshold for workers than other populations is unjustified under TSCA.	• 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 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. • EPA did not consider background exposure that workers and consumers using products containing MC might be exposed to in addition to exposures from TSCA-regulated conditions of use. This may result in an underestimation of risk, and additional discussion of this underestimation has been added to the document in the Key Assumptions and Uncertainties section.
Estimation of ONU exposures		
SACC	**SACC COMMENTS:** • EPA should consider the different categories of ONUs potentially at risk from exposure to MC at the different conditions of use (e.g., workers who do not handle MC directly, but whose job requires them to be in the same area as users; cleaning staff who can be exposed after hours to residues present in the work area, or office/managerial workers who could be incidentally exposed when visiting a work area but are not at risk from exposure routinely) because their potential exposure risk likely varies.	• EPA does not have reasonably available information and data to consider different categories of ONUs or to develop additional scenarios for ONU exposures. • EPA has included all modeling opportunities with the data reasonably available. We do not have reasonably available info to further differentiate ONU population for the purpose of risk assessment. More data are required to pursue additional modeling options. • In Uncertainties section 4.3.2.1, EPA added the uncertainty "ONUs are likely a heterogeneous population of workers, and some could be exposed more than just occasionally to high concentrations." • For full shift exposures, EPA assumes 8 hours of exposure except when 12-hour shifts apply.

	• Develop scenarios for ONU conditions of use that are amenable to modeling their exposures using assumptions informed by professional judgment and/or information provided by users. • ONUs are likely a heterogeneous population of workers, and some could be exposed more than just occasionally to high concentrations. This possibility should be included explicitly as a source of uncertainty. • Several Committee members suggested EPA assume 8 hours of exposure duration for central tendency workers and ONUs.	
SACC, 72, 75	**SACC COMMENTS:** • In Section 2.4.1.2.2 (p. 117, lines 2114-2119), ONU area monitoring data were available, but were not used. Instead modeling was used to estimate ONU exposures. • ONU monitoring data should have been compared to the modeled estimates and justification provided if it is not possible to do a comparison. Additional discussion is needed on the representativeness or lack thereof of the data. When both monitoring and modeling estimates are available, the most conservative estimate should be used. **PUBLIC COMMENTS:** • EPA has no ONU-specific data and calculates ONU risks based on the central tendency (50th percentile) of worker inhalation exposures as opposed to collecting ONU-specific data or using the	• In Section 2.4.1.2.2, EPA clarified that the area monitoring data were not appropriate surrogates for ONU exposure due to lack of necessary metadata, such as monitor locations and distance from worker activities, to justify its use. • EPA compared monitoring data to model predictions for the one OES, Cold Cleaning (Section 2.7.3 of the Supplemental Information on Releases and Occupational Exposure Assessment), for which both were available. EPA has added explanation to section 2.4.1.2.7 to explain that monitoring data have higher weight of evidence due to higher relevance than modeling results for this use for several reasons: (1) monitoring data are known to be relevant to this use; and (2) the modeled results cannot be validated and do not capture the full range of possible exposure concentrations identified by the monitoring data for this use. For example, the 95th percentile modeling results appear equal to about the 25th percentile of monitoring data. • For most occupational exposure scenarios, ONU-specific data and modeling are not available; in these OESs, EPA assumes ONU exposures are equal to central tendency (50th percentile) of worker inhalation exposures.

	higher end exposure estimates as EPA does for other workers.	
SACC, 66, 72, 73, 70	**SACC COMMENTS:** • Unless use of MC is physically sequestered from other MC-releasing jobs in the same area, the assumption that ONUs are less exposed than users is not sufficiently supported. • The evaluation should expand the descriptions to show physical sequestration of MC from other sources in the same work area or add UFs for these scenarios where more than one user is present. **PUBLIC COMMENTS:** • There are scenarios where ONUs may have almost equal exposure including handling MC in small areas that are poorly ventilated. • The ONUs exposure is underestimated. There might be an interaction between occupational exposure and consumer exposure. • The TURA program reports several instances where ONUs were in close proximity to workers, and without the protection of PPE. • 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 states "The assumption that ONUs are present only in the far-field could result in underestimates for ONUs	• EPA does not have reasonably available data or information on physical sequestration of MC from other sources in the same work area. EPA also has no method to quantify uncertainty factors for scenarios where workers and ONUs are both present. • EPA does not have reasonably available data or information on scenarios where ONUs may have almost equal exposure including handling MC in small areas that are poorly ventilated. • 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 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. • Employees doing equipment maintenance are considered by EPA to

	present in the near-field" (p. 373). It is unclear then, why EPA ignores this potential in characterizing ONU exposures. • In lines 1811-1818, EPA stated that the near field does not accurately represent the ONU workers because the ambient concentration of MC closer to them is lower compared to those who directly work with MC. EPA instead modeled ONU exposures using a combination of far-field modeling and area sampling data, since this would more accurately represent ONU exposures. A contradictory conclusion was then made in lines 2125-2127 that "relative exposure of ONUs to workers cannot be quantified."	be workers and not ONUs. Response to a spill would generally be covered by shorter-term exposures. EPA clarified in section 2.4.1.2.2 that relative exposure of ONUs to workers cannot be quantified using modeling. • Exposures for occupational non-users 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 "occupational non-user" category will have high variability depending on the specific work activity performed. It is possible that some employees categorized as "occupational non-user" 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.
SACC	**SACC COMMENTS:** • In the absence of measurements, the Agency could use modeling for estimating ONUs exposures. Models used in industrial hygiene (AIHA, 2009) could be adapted for this purpose using assumptions based on professional judgment and input from users.	EPA has exhausted all modeling opportunities for ONUs with the data that are reasonably available. The specified AIHA models are too limited and do not have necessary parameter sets, particularly use-specific emission rates and zonal volumes and air flow rates, for ONU exposure assessment.
SACC, 72, 73, 70,	**SACC COMMENTS:** • The risk evaluation should examine how ONU risk changes if exposure is estimated using the distance from ONUs to users and the inverse square law. • This method is considered to be a better estimate of ONU exposure than the use of central tendency for occupational users. • Assigning the occupational users central tendency exposure may not be	• ONU distance from users are accounted in the uses with Near-Field/ Far-Field modeling, which is superior to a method that would use the inverse square law. EPA does not have a method to account for air exchange rates for potential use of the inverse square law nor the reasonably available data or information to estimate distance of ONUs from users in the other assessed uses. • 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

	sufficiently conservative, depending on the specific use scenario and the location of the ONU with respect to the user(s). **PUBLIC COMMENTS:** • EPA ignored exceedances of its risk benchmarks for acute, chronic and/or cancer effects by high-end exposures to ONUs for at least 19 of its 65 conditions of use (for examples, see pp. 431, 436, 449).	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.
Sentinel exposure assessment		
73	**PUBLIC COMMENTS:** • EPA did not establish that its so-called sentinel exposure assessments actually reflect "the plausible upper bound of exposure," as required by EPA's regulation, and EPA did not rely on those assessments in its risk characterizations. • While EPA stated that the sentinel exposure was the high-end exposure with no gloves, EPA does not address whether it considers the sentinel exposure to be the high-end exposure with no respirator as well. • To accurately assess "the plausible upper bound of exposure," EPA should consider exposures without any PPE unless EPA can establish that PPE is always used for the particular condition of use. As discussed in Section 1.B, EPA acknowledged that it does not have data sufficient to establish this, and EPA has further acknowledged that it cannot make such an assumption for at least certain occupational exposure scenarios (see Supplement on Releases and	• Language better describing the consideration of sentinel exposure for consumer use evaluations has been added to Section 4.6. It is as follows: For consumer exposures, a range of consumer inhalation and dermal estimates for each consumer condition of use were provided by varying duration of use per event, amount of chemical in the product and mass of product used per event, while retaining central-tendency inputs for exposure factors and exposure setting characteristics. In presenting the inhalation results, high intensity use was characterized by the model iteration that utilized the 95th percentile duration of use and mass of product used (as presented in U.S. EPA (1987)) and the maximum weight fraction derived from product specific SDS, when available. Dermal exposures for high intensity use were characterized by the model iteration that utilized the 95th percentile duration of use and maximum weight fraction." • The EPA defines sentinel exposure as "the exposure to 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)." In terms of this risk evaluation, the EPA considered sentinel exposure the highest exposure given the details of the conditions of use and the potential exposure scenarios. Sentinel exposures for workers are the high-end no PPE scenario within each OES.

	Occupational Exposure, e.g., pp. 115, 116).	
Coordination with CAA		
67	**PUBLIC COMMENTS:** • EPA itself has adopted a number of national emission standards that limit emissions of MC, which is a HAP listed in CAA § 112. Under CAA § 112, these standards must ensure an "ample margin of safety to protect public health." Thus, if the risk of concern was significant, EPA would have to adopt more protective standards under the CAA. • These standards include, notably, the NESHAP for paint stripping and miscellaneous surface coating operations at area sources. • The draft risk evaluation is deficient in that it fails to draw on the information available to EPA to evaluate use and exposure information. EPA has adopted NESHAPs for many applications restricting emissions of MC, for which it relied on exposure assessments showing concentrations below 25 ppm. • The exposure data in the draft risk evaluation also predate the compliance dates of the NESHAPs (mostly ranging from 2008 to 2011). It is remarkable that the draft risk evaluation was apparently compiled without utilizing the data already in the hands of EPA and other permitting authorities.	• NESHAPs are air regulations that require companies to keep certain records; however, these data are retained at the company sites and are not available in a centralized database. This comment may be in reference to the National Emissions Inventory (NEI), which is compiled every 3 years for the purpose of supporting residual risk evaluations as required by Section 112 of the CAA. NEI contains air emission estimates, which can be estimated by sites using a variety of methods, such as emission factors, mass balance, stack monitoring. A site could use purchasing records and disposals to estimate air emissions, but these purchasing records and disposals are not reported to NEI.
Exposure characterization needs sensitivity analysis		
66, 67	**PUBLIC COMMENTS:** • The MC exposure characterization would	Regarding occupational inhalation exposure modeling, qualitative sensitivity analysis sections were added to Appendix F of in the

	be strengthened by qualitative and/or quantitative sensitivity analysis. A qualitative assessment would help explore potentially influential exposure factors and justify EPA's approach. A quantitative analysis would allow for interpretation of the contribution of individual parameters to the predicted exposure concentrations.	Supplemental Information on Releases and Occupational Exposure Assessment.
Tables in Appendix F of "Supplemental Information on Releases and Occupational Exposure Assessment"		
SACC	**SACC COMMENTS:** • Table Appendix F-1 of "Supplemental Information on Releases and Occupational Exposure Assessment" (p. 270) shows that a discrete distribution was used for weight fraction. However, the actual text reads as if the weight fraction was determined by sampling from two separate distributions with the sampling from the second dependent on the sampling from the first distribution. • Additionally, this table does not show a distribution for New Jersey (number of brake jobs per work shift). No justification is provided as to why this was not considered a variable with an appropriate discrete distribution assumed. • Table Apx F-1 of "Supplemental Information on Releases and Occupational Exposure Assessment" should be updated to more clearly represent what was actually done. • Table Appendix F-3 of "Supplemental Information on Releases and Occupational Exposure Assessment" (p. 280) shows a lower bound for the vapor	• The aerosol product weight fraction of MC was modeled using a two-dimensional sampling technique. A uniform distribution is used to simulate the weight fraction of MC in each aerosol product. Due to lack of data on volumes or market penetration of each individual aerosol product, EPA assumes each aerosol product has an equal probability of being used at any given shop. Therefore, a discrete distribution is used to model the frequency of occurrence of each product, where each product has a probability of occurrence of 10% (there is a total of 10 products). On each iteration of the simulation, the model executes each product's weight fraction distribution and the product frequency distribution. The model then reads the product selected from the product frequency distribution and selects the weight fraction that was generated from the corresponding product's weight fraction distribution. EPA added additional clarification in Section F.1.2.7 and the table. • The number of brake jobs per shift is calculated from the fixed average number of brake jobs per year per shop (this is the only data EPA identified). To calculate NJ, the model uses a constant 936 jobs/site-yr, a constant 8 hr/shift, a constant 52 weeks/year, and a distribution for the number of operating hours per week. Therefore, NJ is varied according to a distribution dictated by the distribution of operating hours per week. This is calculated in situ in the model. • Tables F-3 and F-7 show the value for vapor generation rate at different levels of precision, but the model stores the value at 15 digits

	generation rate of 0.015, but the text describing this parameter (p. 285) gives a value of 0.02. • This table and/or associated text should be updated to represent the correct value. • EPA should revise the risk evaluation and supplemental documents to verify that values for parameters in tables and the text are all reported to the same precision as used in calculations and models. • The distribution for the exposure duration parameter in Tables Appendix F-3, F-4 and F-5 (in Appendix F of "Supplemental Information on Releases and Occupational Exposure Assessment," pp. 280, 281, and 282) is given as being a discrete distribution; however, the text describes this parameter as being determined based on the number of operating hours per day. Both could more accurately be listed as a constant or as a calculated value based on the number of operating hours.	of precision. EPA updated the value in Table F-7 to 0.015. • EPA revised the tables to clarify exposure duration is calculated from operating hours per day.

Human Health Hazard
EPA used the acute point of departure (POD) to use to estimate risks from the human controlled experiment described by Putz et al. (1979). This study was rated as a medium quality study; it was a double-blind design but used a single exposure, which prevented the use of dose-response modeling. Given uncertainty regarding concentrations and exposure durations and the potential for a steep dose-response leading to death as suggested by these case reports and the analysis by Benignus et al. (2011), EPA considers Putz et al. (1979) to be the most relevant study for this risk evaluation. **Charge Question 5.1.** Please comment on the appropriateness of the approach, including the data quality evaluation, and the approach's underlying assumptions, strengths and weaknesses. **Charge Question 5.2.** Please provide any specific suggestions or recommendations for alternative approaches that should be considered by the Agency in characterizing the acute inhalation risks. **Charge Question 5.3.** Please provide relevant data or documentation and rationale for including other studies and endpoints for

consideration.

Charge Question 5.4. Please comment on the severity of the response used as the basis of the POD as well as the use of the result at 1.5 hours rather than at 4 hours.

For methylene chloride, exposure-versus-time data are limited. Therefore, EPA considers the Ten Berge equation using n = 2 as a valid method to convert the 1.5-hr POD value from Putz et al. (1979) to the 15-min, 1-hour and 8-hr PODs.

Charge Question 5.5. Please comment on the conversion of the 1.5 h time point in Putz to 15 min, 1-hour and 8-hour PODs.

EPA used PODs and cancer slope factors (i.e. human equivalent concentration (HEC), inhalation unit risk (IUR) and dermal slope factor) for evaluating the non-cancer and cancer risks, respectively, for chronic exposures to methylene chloride.

5.6. Please comment on the appropriateness of the approach, including its underlying assumptions, strengths and weaknesses.

Charge Question 5.6. Please comment on the appropriateness of the approach, including its underlying assumptions, strengths and weaknesses.

Charge Question 5.7. Please provide any specific suggestions or recommendations for alternative approaches that should be considered by the Agency in characterizing the chronic inhalation risks to workers.

Charge Question 5.8. Please provide relevant data or documentation and rationale for including other studies and endpoints for consideration.

EPA used a linear low-dose extrapolation for evaluating potential cancer risks from chronic exposures to methylene chloride.

Charge Question 5.9. Please comment on the appropriateness of using a linear low-dose extrapolation versus a non-linear or threshold approach, recognizing that methylene chloride is predominantly metabolized by cytochrome P450 2E1 to carbon monoxide at low concentrations (a high affinity, low capacity pathway) and by glutathione S-transferase T1-1 to two reactive intermediates (i.e., S-(chloromethyl)glutathione) and formaldehyde) at high concentrations (a low affinity, high capacity pathway).

EPA calculated a cancer slope factor by using a PBPK model that accounts for the internal dose of the amount of methylene chloride metabolized through the glutathione S-transferase T1-1 (GST) pathway.

Charge Question 5.10. Please comment on the appropriateness of applying the PBPK model and assumptions within the model, specifically using the internal dose metric of daily mass of methylene chloride metabolized via the GST pathway as the basis for performing a linear low-dose extrapolation for quantifying potential cancer risks from chronic exposures to methylene chloride.

#	Summary of Peer Review Comments for Specific Issues Related to Charge Question 5	EPA/OPPT Response
Acute PODs		
SACC	**SACC COMMENTS:** • The Committee was generally satisfied with the approach of using the 1.5-hour result from Putz et al. (1979) as the basis of the acute POD; however, one Committee member felt that the modest CNS effects are more useful in establishing a LOAEL and recommended the Agency use the 4-hour	EPA believes that effects at the 1.5-hr time point are important; this was the first time point that a statistically significant change was observed. Although the effect was a 7% change in a visual response as part of a dual performance task, EPA adjusted the LOAEL to NOAEL uncertainty factor to 3 (from a default of 10) to account for the lower severity of effect. Longer studies are described in the MC risk evaluation. Although

	exposure level of 200 ppm to convert to the 15-minute, 1-hour and 8-hour PODs. • The Committee suggested the risk evaluation should support conclusions by including data from other human studies measuring CNS effects from longer duration exposures than are summarized in this risk evaluation.	studies are available for longer durations and do suggest effects on the nervous system associated with MC, they were not adequate for risk evaluation. Lash et al. (1991) identified a lower score on attention tasks and complex reaction time from MC exposure, but this effect was not statistically significant and could have been affected by other pollutants. Cherry et al. (1983) also identified neurological changes but received an unacceptable data quality rating. General Electric Co (1990) found a statistically significant effect associated with 49 ppm MC but did not control for other chemical exposures. These studies are already described in the risk evaluation.
67	**PUBLIC COMMENTS** • While this Putz et al. (1979) was considered to be of medium quality in the systemic review, only one exposure concentration was tested, which is a significant issue for assessing the acute neurobehavioral effects of MC because the dose-response curve cannot be determined.	Although EPA would have preferred to use a study with multiple exposure concentrations, Putz et al. (1979) was superior to the other studies for several important reasons. First, Stewart et al. (1972) also used only one concentration per experiment, but with higher concentrations than Putz et al. (1979). Second, Winneke (1974) provided only limited dose-response information (one or two concentrations per experiment), and the responses at 300 ppm were similar to or sometimes more pronounced than at 500 ppm. Although Gamberale et al. (1975) conducted their experiment using four concentrations, effects were observed only at 1000 ppm; yet, Gamberale et al. (1975) received a 'low' data quality rating and among all of the acute human experimental studies, the majority of individual experiments at lower concentrations showed some effect of visual and auditory responses. For these reasons, EPA considered it important to use Putz et al. (1979), which did report the lowest concentration associated with an adverse effect. In addition, CNS depression is identified in multiple studies in humans and animals. Furthermore, serious effects (including lethality) are observed at higher concentrations, with limited information regarding the concentrations where lethality occurs.
45, 67	**PUBLIC COMMENTS:** • EPA's acute toxicity assessment is	EPA applied risk assessment methods tailored to the needs of TSCA implementation. TSCA compels EPA to evaluate risk associated

	inconsistent with existing occupational exposure limits (OELs) (8-30-fold lower than the current range of widely accepted 8-hour TWA OELs from 25 to 100 ppm). • Neurological effects were not reported in occupational cohort studies, with MC exposures in the range of OELs. • Human kinetic studies by DiVincenzo and Kaplan (1981) indicate that exposure to 100 ppm MC for 8 hours would result in a COHb blood level of approximately 3%, which is the NOAEL for neurobehavioral effects based on Putz et al. (1976). • Data indicate that exposure to OEL levels would not increase COHb levels above background or result in COHb above the NOAEC for CO, including for susceptible individuals lacking the GST-T1 enzyme.	with specific conditions of use without consideration of cost or other non-risk factors. Occupational risk assessments and conclusions are performed for a different purpose using a different set of assumptions and considerations. OSHA specifically notes that they considered issues of feasibility in choosing both the PEL of 25 ppm and 15 min STEL of 125 ppm and acknowledges that there are still risks associated with both of these values (OSHA, 1997). Actually, some indications of neurological effects have been seen in multiple longer-term studies. General Electric Co (1990) identified dizziness and vertigo associated with 49 ppm MC. Lash et al. (1991) found some association between MC and lower scores on attention and reaction time tasks; there was a lack of statistical significance but sample sizes were low. Although considered unacceptable due to participants' loss to follow-up, Cherry et al. (1983) identified sleepiness, tiredness, mood change and deterioration on digit symbol tests associated with MC. Finally, although Silver et al. (2014) did not identify deaths from malignant or non-malignant diseases of the nervous system, this endpoint is much more severe compared with responses used for the acute timepoint. EPA expects that direct exposure to the parent compound MC will also result in CNS effects, based on human experimental studies. Two studies (Putz et al., 1979; Winneke, 1974) separately tested MC and CO concentrations (with both MC and CO expected to result in the same COHb levels) and had identified more CNS effects associated with MC (and no CNS effects were associated with CO in one study). Thus, COHb is not the only compound producing CNS effects associated with MC exposure. EPA agrees that COHb levels even down to 2% may result in exacerbation of cardiotoxicity. For example, in Section 3.2.4.1, (Weight of Scientific Evidence, Non Cancer), EPA identified studies of COHb levels ranging from 2 to 4.5% that have resulted in decreased time to onset of angina pain during exercise among individuals with coronary artery disease. Because there is little evidence of this effect directly associated with MC but because it

		may occur as a result of increased COHb concentrations from MC exposure, EPA has included an uncertainty factor to account for possible exacerbation of cardiac effects.
73, SACC	**SACC COMMENTS:** • The Committee questioned the conclusion in the risk evaluation that the MC-induced CNS effects are concentration-dependent with a steep dose-response curve. • Recommendation: Use the data from the Winneke et al. (1974) study to confirm the assumption used in the dose-response modeling of the Putz et al. (1979) study. **PUBLIC COMMENTS:** • The commenter supported use of Putz et al. (1979) because it provides better study quality and a more health-protective POD for the draft risk evaluation.	**Response to SACC Comments:** EPA evaluated information within Winneke (1974) more fully and also reviewed other information to more fully consider the steepness of the dose-response curve. Information from the human experimental studies is inconclusive/not supportive of a steep dose-response curve in the range of concentrations from these studies (see Appendix B, below). However, lethality data in animals is supportive of a steep dose-response curve because these studies show an increase in mortality from 0 to 100% within an approximately twofold increase in exposure concentration, with death primarily preceded by CNS effects (Nac/Aegl, 2008). In addition, although EPA doesn't have definitive information on concentrations associated with human deaths, information suggests that in one report, lower exposures (e.g., down to 100 ppm or lower) *might* have been associated with lethality. In conclusion, the lethality data in animals and the potential that human lethality may occur within the range of concentrations associated with less severe effects still support EPA's statement regarding the fact that there may be a steep dose-response leading to lethality. The study used for the POD has only one concentration so there is no dose-response information within that study. **Response to Public Comments:** Agreed.
Comments on use of Ten Berge approach for acute POD		
SACC	**SACC COMMENTS:** • Check calculations for the 1- and 8-hour PODs to ensure that no impactful rounding is occurring.	EPA has updated the process used for rounding and has also updated the risk estimates.
SACC, 67, 73, 45	**SACC COMMENTS**: • One committee member supported the use of the ten Berge equation but noted there are additional relevant models. Committee	EPA understands the uncertainties in using any model, including the use of lethality data for non-lethal effects. However, when weighing the scientific evidence, EPA chose the use of the ten Berge equation of $C^{\wedge n}$ *T, where n = 2 instead of other approaches because even

	discussion pointed out that the ten Berge equations have limitations. The work of ten Berge (1986) was limited to data on lethality and often does not accurately reflect dose-response relationships for very short periods of exposure, as well as for longer durations (Bruckner et al., 2004). Use of the Cnxt approach can underestimate longer AEGLs and thereby overestimate risks. • Recommendation: Use the PBPK model for acute exposures or justify why it is not suitable for this task. The Committee described the PBPK model as both more scientifically justifiable and more protective of human health. • Additional advantages were identified for using PBPK modeling over the ten Berge equation. It should be recognized that blood and brain concentrations of MC increase rapidly upon initiation of inhalation exposure, approaching near steady-state, or equilibrium within 1.5-2 hours. CNS depression is directly attributable to the parent compound. Human PBPK modeling and monitoring data show gradual, progressive increases in blood MC levels over the next 6 hours of exposure (Bos et al., 2006). For duration adjustments, NAS (2009) used a PBPK model based on a modification of the model of Andersen et al. (1987, 1991) and by Reitz et al. (1997). NAS (2009) utilized the same modeling to simulate COHb levels for derivation of AEGL-2 values. **PUBLIC COMMENTS:** • EPA's use of the ten Berge et al. (1986)	though the lethality data are not ideal, they do represent an empirically-derived value from inhalation data for solvents that can be used for n. There are also several reasons that EPA did not use the PBPK model, as described below. Although the PBPK model described by Bos et al. (2006) and used to set AEGLs seems appropriate for these higher emergency guideline values, EPA believes that there are enough uncertainties regarding both the assumptions used in the model and the validation of the model that don't warrant using it *instead of* the ten Berge equation for the lower acute PODs in the current risk evaluation. Although the model accounts for P-450 saturation and thus, a switch to metabolism/conjugation by GSTT1, P450 saturation occurs at approximately 500 ppm, which is higher than the POD for the current evaluation. In addition, the model includes the distribution of GSTT1 in the population; this refinement may not be entirely necessary when using human volunteers (especially at lower MC concentrations). Furthermore, the parent compound has been shown to result in CNS effects that are in excess of CO/COHb concentrations, as identified by Putz et al. (1979) and Winneke (1974). However, Bos et al. (2006) acknowledge that there are no adequate data on MC in rat or human brains and also assumes that at longer exposures, the more relevant endpoint is COHb only. OSHA, when considering a similar PBPK model for acute effects for derivation of the 1997 PEL, had similar concerns the about lack of experimental validation of the predicted brain MC concentrations and the level of brain concentrations that would produce detectable CNS depression (OSHA, 1997). Although EPA understands that the COHb concentrations may be maintained for several hours after exposure ceases (and a primary reason to consider this type of PBPK model), this effect is not as pronounced at lower concentrations. Finally, Bos et al. (2006) state that the model overpredicts MC and COHb concentration by up to 50%; thus, the lower POD predicted by the model for longer exposure durations may be partially due to this overprediction.

	equation and UFs is untenable in light of the MC human kinetic data and the PBPK models. EPA's assertion that the values derived from differing methods (i.e., ten Berge equation vs. PBPK model) are "similar" is inaccurate and fails to acknowledge that the differences are non-negligible. The application of time averaging in the ten Berge calculation may not fully consider the toxicokinetic data for MC or the concentration-response data for the selected endpoints. • Because the human behavioral effects can be caused by both hypoxia (COHb levels) and by the MC brain concentrations, which exhibit different kinetics and thus different dose-response relationships over time, a PBPK model (published by Bos et al., 2006) was used to derive ATSDR's acute oral Minimal Risk Level (MRL) and EPA's AEGL values (Reitz et al., 1997; AEGL, 2009). The PBPK model also incorporates the impact of the GST-T1 polymorphism in humans. In the draft risk evaluation, however, EPA did not use these models.	For the final risk evaluation, EPA added a 12-hr time point; to consider the sensitivity of using n = 2 in the ten Berge equation for this longer time point, EPA extrapolated to this time point using both a value of n = 1 and n = 2. In conclusion, although the PBPK model may be an important way to account for the time-course of sustained COHb levels at higher AEGL values, EPA believes that it doesn't add enough value over the use of the Ten Berge et al. (1986) approach for the current risk evaluation. EPA has added more information to the risk evaluation to describe uncertainties related to the PBPK model as well as any uncertainties in not using the model.
Acute exposure and cancer		
73, 75	**PUBLIC COMMENTS:** • EPA's risk evaluation should account for acute cancer risks to workers and consumers. It is widely recognized that genotoxic carcinogens like MC can induce cancer following a limited acute exposure event and that methods to estimate such risks are available (NRC 1993a). • As stated in this NRC report, the decision to conduct extrapolation and modeling should	For the current MC risk evaluation, there is a significant database of positive mutagenicity results for the MC metabolites of the GST pathway, particularly related to the GSTT1 isozyme. EPA believes that these data are strong enough to model cancer using a linear low dose extrapolation. However, there are still some uncertainties regarding the strength of the information relate to this MOA. *Standard Operating Procedures for Developing Acute Exposure Guideline Levels for Hazardous Chemicals* notes the significant uncertainty in extrapolating risks from lifetime exposures to shorter

	be based on the "sound biological and statistical principles." There is concern that EPA did not sufficiently consider such principles related to mode-of-action in deciding not to model acute cancer risk based on chronic exposure data. A linear low-dose extrapolation from chronic to acute exposures would be the appropriate approach to take for MC.	(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.
Non-cancer hazards not considered for chronic POD		
SACC, 49, 55, 70	**SACC COMMENTS:** • The Committee considered the potential immunotoxicity of MC to be underestimated, even based on the somewhat equivocal results. • There are a few epidemiological studies included in the risk evaluation that show a weak association, and this is supported with data from short-term animal models. The evidence, especially the results from Arayni et al. (1986), fulfill the NTP criteria for "clear evidence of toxicity to the immune system (NTP 2009)." • The Committee disagrees with study quality rating for the Arayni et al. (1986) study, which was not rated more highly because of a lack of information about test substance preparation and animal group allocation. • Recommendation: Add a conclusion statement to Section 3.2.3.1.3, Immune System Effects, stating that this summarizes the equivocal results while acknowledging the strong potential for MC immunotoxicity based on the Aranyi et al. (1986) study. **PUBLIC COMMENTS:** • In its MC risk evaluation, EPA "did not carry	**Response to SACC comments:** After closely reviewing the NTP (2009) criteria and the information on immunotoxicity related to MC exposure, EPA considers there to be *some* evidence of immunotoxicity from MC. Although Aranyi et al. (1986) identified a statistically significant decrease in bacterial resistance accompanied by increased mortality at the highest of two MC concentrations, there is a lack of information on the dose-response gradient simply because the effect was seen only at the highest concentration and there are no other similar bacterial resistance studies to show the effects at different concentrations. One human study identified increased mortality from infection, and another identified increased mortality from non-specific chronic bronchitis, but the results are not consistent across studies. Also, other subchronic and chronic animal studies did not identify increased infection rates associated with MC exposure. (NTP (1986) measured this and found an infection in only one low-dose female, and the functional IgM assay was negative. Although EPA did consider the NTP (2009) criteria, EPA also used an evidence integration framework to consider the evidence on MC's association with immunotoxicity (see Appendix A, below). EPA has applied consistent data quality evaluation criteria across studies and considers Aranyi et al. (1986) to be a medium quality study, which is an acceptable confidence rating.

	immune system effects forward for dose-response" analysis "due to a limited database" of immunotoxicity studies. The evidence that EPA does have, however, indicates that MC is immunotoxic.	EPA added more information to the conclusion section for the immunotoxicity endpoint. **Response to public comments:** EPA considers the database to show some evidence of immunotoxicity and has revised the hazard identification and weight of the scientific evidence sections.
	PUBLIC COMMENTS: • The agency should present a more defensible rationale for dismissing the ASD endpoint based on a single study limited to one county in one state when four other studies consistently present evidence of an effect. • Lack of a link to specific conditions of use does not provide a basis for exclusion of studies for use in dose-response assessment. • The lack of an animal model for ASD should not preclude the inclusion of epidemiologic evidence, given that humans are the species of interest.	EPA acknowledges the hazard associated with the ASD endpoint, including the low air concentrations that are associated with consistently positive odds ratios (e.g., several hundred ng/m3). However, given uncertainties already described regarding the models, EPA has chosen not to calculate risks for ASD. EPA agrees with this statement. Lack of a link with specific conditions of use should not be a basis for exclusion because animal toxicity studies are used in risk evaluations and they cannot be linked to specific conditions of use. However, the risk evaluation doesn't make this claim. The weight of scientific evidence section (Section 3.2.4) for the ASD studies does, however, note that the studies do not provide exposure estimates for workers (e.g., nurses) or indoor exposure estimates for consumer products or indoor exposure estimates for the general population. This statement refers to the fact that these other possible MC exposures may suggest that these studies may not fully account for all MC exposures. EPA added clarifying language to the Sections 3.2.4.1.4 and 4.3.5 (Weight of Scientific Evidence and Key Assumptions sections). EPA agrees that the ASD studies can be considered on their own merit. Yet, EPA has considered the available information in drawing conclusions regarding this endpoint and has noted the lack of applicable animal data for MC.
73	**PUBLIC COMMENTS:** • EPA's decision to ignore human evidence of hematologic effects results in a less protective risk metric. The California EPA	Two human experimental studies found greater CNS effects from the parent compound MC than from CO (both resulting in the same COHb concentration). Therefore, EPA doesn't recommend basing a value on modeling only COHb. (See a more complete response

	(CalEPA) based its 2008 chronic Reference Exposure Level (REL) on a human study (DiVincenzo and Kaplan, 1981) and arrived at a more protective result than did the draft risk evaluation's approach.	regarding COHb in the second row – commenters 67, 73, 45 - under "Comment on use of ten Berge approach for acute POD.") EPA chose an intraspecies uncertainty factor to address individuals with cardiac disease who may have decreased time to angina at COHb levels lower than those associated with the acute POD for MC.
49, 55, 72	**PUBLIC COMMENTS:** • In a risk evaluation, a decision not to further analyze an endpoint has the same effect as a finding of unreasonable risk. EPA's risk management rules for MC will not address immune system, developmental, or reproductive effects because EPA has neglected its responsibility to evaluate whether and at what levels those risks are unreasonable.	EPA presented and analyzed the reasonably available information for immune system, developmental, and reproductive effects in the hazard identification and weight of evidence sections in the risk evaluation. Based on the weight of the scientific evidence, EPA decided not to advance these data to the dose-response analysis. Unless otherwise indicated, an endpoint subject to "no further analysis" in risk evaluation may be included in the risk evaluation and when EPA makes its unreasonable risk determinations as to whether methylene chloride presents unreasonable risk under the conditions of use based on an endpoint this also includes other endpoints.
55, 73	**PUBLIC COMMENTS:** • MC has enough toxicity data to show that it exhibits developmental toxicity and neurotoxicity. EPA should regulate it as a developmental neurotoxic agent, with potential lasting adverse effects on neurological functioning. • EPA must act immediately to fill the data gap for developmental neurotoxicity.	As noted, some studies have identified neurotoxicity and some developmental toxicity. EPA considers the database to be adequate for evaluation and used reasonably available information to assess these endpoints in a weight of scientific evidence analysis to identify a developmental neurotoxicity hazard but did not bring the information forward to dose-response for a variety of reasons discussed in Section 3.2.4 of the Risk Evaluation.
49, 55	**PUBLIC COMMENTS:** • EPA does not evaluate endocrine effects in either of the draft risk evaluations and has not determined whether MC presents an unreasonable risk of endocrine disruption, or otherwise addressed in the risk evaluation, as a data gap.	EPA evaluated the outcomes from existing epidemiological and toxicity studies of MC that might be related to endocrine disruption and considers the database adequate for risk evaluation without the need to separately address endocrine effects on their own.

SACC, 55	**SACC COMMENTS:** • Include more information on irritation and burns. One Committee member dnoted an additional source of information: King County, Washington analyzed poison center data for 2007-2016 for MC (Fisk and Whittaker, 2018). **PUBLIC COMMENTS** • Failing to address irritation and burns will lead to underestimations of risk and leave the public – including families and workers – at risk from illness and disease due to exposure to this toxic solvent.	EPA added information on irritation and burns from Fisk and Whittaker (2018) to the risk evaluation. Air concentrations leading to eye and respiratory tract irritation are not well established. Eye irritation has occurred in rabbits, but this is after direct instillation in the eye. Burns have occurred upon direct contact with skin and eyes, including one worker that experienced severe corneal burns and other anecdotal information that 1st through 3rd degree burns may occur after direct contact EPA added the following statement to Section 4.2 (human health risk characterization) to address the possibility of irritation and burns: "Although irritation and burns may result from exposure to methylene chloride, air concentrations leading to eye and respiratory tract irritation are not well established, nor are concentrations resulting in direct contact burns to skin or eyes."
Chronic POD not protective		
55	**PUBLIC COMMENTS:** • MC chronic toxicity is underestimated. EPA should consider the potential effects of MC at levels much lower than the POD, including effects that may be biologically significant, even if they are not statistically significant. The commenter refers to increased COHb, which was observed down to 50 ppm in Nitschke et al. (1988), the 2-year bioassay used for chronic liver effects. • It may be appropriate to re-calculate the risk estimate using a lower POD or add additional adjustment factors to provide a margin of safety for adverse effects at lower exposures.	EPA evaluated the reasonably available epidemiological and animal toxicity studies for multiple health outcomes and chose the PODs considered to be most appropriate given the data quality evaluations, amount of data reasonably available and integration of the data. EPA considers both biological and statistical significance equally when evaluating adverse effects and conducting dose-response modeling. This is highlighted in *Benchmark Dose Technical Guidance* (EPA, 2012a), which notes the need for a statistical or biological trend when considering dose-response modeling and even on EPA's website (www.epa.gov/risk/conducting-human-health-risk-assessment), which defines the NOAEL as "the highest level at which no statistically or biologically significant increases are seen in the frequency or severity of adverse effect." Even though biological significance is of importance, however, it cannot always be easily established (e.g., the percent response of a given endpoint that is adverse is not always well established). EPA agrees that increased COHb levels may result in exacerbation of cardiotoxicity (decreased time to angina pain) and increased

		levels are expected to contribute to CNS depression, although the exact contribution is unclear (see Putz et al. (1979) and (Winneke, 1974), showing less or no CNS effects from CO). Therefore, EPA uses the intraspecies uncertainty factor to account for susceptible subpopulations associated with this effect (e.g., decreased time to angina for individuals with cardiac disease).
55	**PUBLIC COMMENTS:** • How will EPA treat data where a dose-response trend includes lower doses that do not achieve statistical significance? How will EPA treat an outcome that may not have statistical significance, but has biological significance? How will EPA treat data that are limited by some potential confounding factors, but show consistence across studies? How will EPA include studies with outcomes that are difficult to quantify, but have biological significance? • In the face of scientific uncertainty, rather than obtaining the data needed to answer pending questions as the law requires, EPA has instead disregarded and dismissed evidence of harm.	When conducting benchmark dose (BMD) modeling, EPA fits data from all doses in a study, regardless of whether they all were statistically significantly different from the control response. Therefore, the doses that were not statistically significant are included and inform the modeling. EPA relies heavily on the biological significance by choosing *a priori* the response that will be the basis of the BMDL, although oftentimes the response level that would be considered adverse is not available so a standard response level is used. EPA evaluates studies to determine whether confounding factors could substantially affect the outcome of a study; if so, the study might still be considered in the weight of evidence to the extent it can be used but would likely not be relied upon for dose-response modeling. For irritation and burns (endpoints that are difficult to quantify), EPA has identified the possibility that they may result from methylene chloride exposure (see Section 4.2, Human Health Risks) . However, they are not modeled in the risk evaluation due to lack of quantitative information. EPA relied on reasonably available information and considers the database for MC to be adequate for risk evaluation. In particular, the hazard database for MC is fairly robust, but some of the information in the studies is not easily modeled quantitatively.
Reconsider liver POD		
67	**PUBLIC COMMENTS:** • HSIA considers hepatocyte vacuolation in female rats from the 2-year inhalation study	EPA considers hepatocyte vacuolation to be an adverse outcome relevant for humans. Therefore, the study is appropriate for inclusion in the risk evaluation of MC.

	by Nitschke et al. (1988) an inappropriate endpoint for EPA 's POD for chronic non-cancer inhalation exposure. • Perhaps a more appropriate endpoint for a POD for chronic non-cancer inhalation exposure is the genomic changes associated with circadian rhythms observed in liver and lungs of mice exposed by inhalation to MC in the Andersen et al. (2017) study.	EPA has evaluated the information on genomic changes and determined that it is premature to use this information without a more complete understanding of the key events associated with adverse outcomes. EPA added discussion of Andersen et al. (2017) to the cancer weight of scientific evidence section.
Use of body weight scaling on BMDL10 predictions		
SACC	**SACC COMMENTS:** • One Committee member questioned use of body weight scaling on animal BMDL10 predictions. Given that there is uncertainty regarding differences in clearance, then it seems that using an UF of 3 for pharmacokinetic differences would be a more consistent approach to addressing this uncertainty. • Even if body weight scaling is used, it should be applied after the model is used to get the human external doses. • It would be useful if more detail was added on how the sampling for the GST-T1 polymorphism was conducted (Appendix I, p. 659, lines 11601-11603).	EPA doesn't apply uncertainty factors when using the cancer slope factor derivation; therefore, $BW^{3/4}$ is considered the only approach to address animal to human extrapolation uncertainties when data are limited. For non-cancer, $BW^{3/4}$ was applied (table 3-19) to the animal $BMDL_{10}$ to obtain a value of 130.0 (see Table 3-19). Because the relationship (as shown in the Toxicological Review; Fig 5-7) is linear, applying $BW^{3/4}$ before or after the HEC calculations doesn't make a difference. EPA $BW^{3/4}$ policy gives preference to $BW^{3/4}$ rather than an uncertainty factor of 3 to account for animal to human TK extrapolation. Using a 3x uncertainty factor results in a similar, slightly lower POD. EPA added details regarding the GST-T1 sampling to the risk evaluation.
Evaluation of cancer epidemiology data		
SACC	**SACC COMMENTS:** • Limitations in the evaluation of epidemiological studies and the "healthy worker effect" were noted. • However, the other biases, namely the healthy worker survivor bias, can occur when workers with poorer health status continue to leave the workforce or switch jobs and as a result incur lower exposures. Unlike the	EPA added details regarding the healthy worker survivor bias to the weight of evidence section for human health.

	healthy hire bias, this cannot be addressed using internal reference groups. • Recommendation: Add further details to the evaluation of the epidemiology studies to fully describe the "healthy worker effect."	
46, 67, 68	**PUBLIC COMMENTS:** • The lack of consistency and absence of associations in well-defined cohorts having experienced high exposures suggest that the carcinogenic hazard of MC to man is low or non-existent. It should not be classified as "likely carcinogenic in humans."	EPA relied on the 2005 Cancer Guidelines (EPA, 2005b) to determine the classification, which considers results from both epidemiological *and* animal toxicity studies to determine the likelihood of carcinogenicity in humans. In addition, several of the epidemiological studies did identify associations between MC and various cancers. Finally, EPA identified methodological issues in epidemiological studies (both more generally and specifically for MC). Several of these issues make it difficult to determine an association between MC and cancer in humans, even if an association may exist.
46, 68, 73	**PUBLIC COMMENTS:** • EPA dismisses human epidemiological studies and disregards their well-accepted value in public health risk assessment. EPA's attempt to summarize specific criticisms and project them upon the broader body of human evidence is unhelpful and misleading. The constellation of inherent limitations presented in the draft risk evaluation appears to lean toward an interpretation that true positive associations somehow were missed. • The agency should instead apply specific criticisms where applicable to its discussion of individual studies and focus its assessments of the WOE on the strengths and limitations on the entire study database.	EPA added more information to the risk evaluation (Section 3.3.4.2) to address the epidemiological database as a whole including discussion of the healthy worker effect (survivor bias). EPA believes there is value in describing possible limitations that may make it difficult to discern positive associations. However, EPA has also described situations where possible positive associations may actually be overstated due to confounding by other chemicals.
67	**PUBLIC COMMENTS:** • EPA is to be congratulated for a much more realistic interpretation of the epidemiology data base for MC. We question the characterization of "inconclusive" results as	Thank you for your comment.

	"limited" evidence of anything, but otherwise commend EPA's recognition that the cohort studies do not show a cancer risk.	
67	**PUBLIC COMMENTS:** • The cohort studies have many features that make them useful for evaluating potential health effects associated with MC. Considered as a whole, the available epidemiological evidence does not indicate a cancer risk associated with occupational exposures to MC. The studies consistently demonstrate no excess mortality for all causes of death, total cancer, and the cancers that were observed in the one positive mouse bioassay (lung and liver cancers). • Moreover, a recently published comprehensive study of chlorinated solvents and brain cancer found no association between exposure to any of six chlorinated solvents, including MC, and glioma risk (Ruder et al., 2013). • In conclusion, the absence of associations in well-defined cohorts having experienced high exposures suggests that the carcinogenic hazard of MC to man is extremely low or non-existent, as summarized in the review by Dell et al. (1999). The strong and consistent cohort studies showing no increase in cancer risk should accordingly be determinative in characterizing that risk.	EPA agrees that it is important to consider the cohort studies. However, several epidemiological studies did identify associations between MC and various cancers. Also, EPA identified methodological issues that may make it difficult to measure the association between MC and cancer in humans as identified in the risk evaluation. EPA described the results of Ruder et al. (2013) in this risk evaluation. EPA has considered all of the studies, including the cohort and case-control studies. As noted in the risk evaluation, most of the cohort studies used SMRs or standard incidence rates (SIRs), which use rates from the full population; therefore, there are possible important differences between the workers and the comparison group. Thus, even though the cohort studies have some strong attributes, EPA doesn't believe that they are determinative by themselves and need to be considered with the case-control studies as well as the animal and mechanistic data.
Epidemiological data – application of systematic review		
SACC	**SACC COMMENTS:** • The Committee recommends improvement of the systematic review process, including the definition and use of "unacceptable" studies in TSCA risk evaluations. The Committee	EPA has outlined specific criteria for identifying a study as unacceptable in *Application of Systematic Review in TSCA Risk Evaluations*. Note that EPA considered single dose studies as not *relevant* (vs. unacceptable from a quality perspective) when considering studies for the dose-response process; they were

	reiterates that single dose studies can contain useful information and should not be ranked "unacceptable" just for having a single dose. • Recommendation: Develop quality assessment criteria for human studies to be included in its systematic review methods prior to review by NAS.	excluded during the screening steps. However, previous studies in authoritative sources (e.g., the IRIS assessment) were sent forward for data evaluation regardless of whether they were a single dose study. EPA will develop criteria for human experimental studies for upcoming assessments.
73	**PUBLIC COMMENTS:** • The rationale presented for certain ratings within influential criteria is inadequate or flawed, thus negatively influencing the agency's confidence rating of particular studies. For example, the agency concluded that relying on National Air Toxics Assessment (NATA) data for exposure measurements was insufficient with respect to the relationship between exposure and autism spectrum disorder for four epidemiological studies.	EPA revised the discussion of the NATA data in the weight of scientific evidence section (Section 3.2.4.1.4) to focus primarily on the concern related to some of the studies that used multiple years of NATA data. Although EPA had previously suggested that exposure data specific to individual months as used by von Ehrenstein et al. (2014) might be more closely aligned with vulnerable exposure periods, stronger associations have been identified for the first year of life in one study of pesticide exposure compared with prenatal exposures, suggesting the *potential* that a full year (and the first year of life) may be an important developmental period (von Ehrenstein et al., 2019).
Cancer hazard evidence integration		
SACC	**SACC COMMENTS:** • The lack of evidence for cancer risk in epidemiological studies is not compelling. Humans are so genetically variable, with so many other exposures and complicating issues, that it is difficult and often rare to find associations in epidemiological studies. • Animal studies reveal a clear association with liver cancer. In terms of lung cancer, there is clear evidence of a link in animals exposed via inhalation, and some evidence for oral exposure. There is some evidence of a link between MC exposure and breast cancer in animals. Consequently, it made sense to use the animal data for the risk evaluation.	Thank you for your comment. EPA agrees that the use of animal data is appropriate in this risk evaluation.

41, 45, 46, 56, 68, 44	**PUBLIC COMMENTS:** • Regarding potential cancer risks, there are several medium to high-quality epidemiological studies available for occupational populations, which do not demonstrate evidence of carcinogenic hazard. Yet, these studies were deemed "uncertain" and "inconclusive" by EPA and largely discarded in the hazard assessment for MC. • Where animal and human (and possibly mechanistic) evidence fail to align, it is clear that more objective and verifiable methods are needed for evidence integration.	EPA has comprehensively evaluated the human and animal studies for MC. Although many epidemiological studies may have been conducted adequately, there are still inherent aspects of some of these studies, such as lack of control for co-exposure to other chemicals that are associated with the same outcome, that make it difficult to either fully understand the true relationship between MC and cancer or use the studies quantitatively in a risk evaluation. However, EPA clearly identified relevant issues and described the logic regarding which endpoints and studies would be considered for dose-response in the weight of evidence section. EPA will work with the National Academy of Sciences, Engineering, and Medicine (NASEM) TSCA Committee to consider revisions to the data quality evaluation criteria and options regarding integrating evidence within and across evidence streams (human, animal, mechanistic data). EPA proposes to use a more structured framework for evidence integration for the next set of chemicals evaluated under TSCA.
The human relevance of mouse tumor data is uncertain		
SACC, 67	**SACC COMMENTS:** • The decision to base the risk assessment on mouse data was questioned, since mice have greater GST-T1 activity than rats or humans and this may make mice more susceptible to getting these types of tumors. • Recommendation: Add information on the relevance of mouse data to humans. • Recommendation: Include a discussion of the issue of whether MC itself or its metabolites (or both) are causing the observed effects. **PUBLIC COMMENTS:** • In light of the draft risk evaluation's sound interpretation of the cancer epidemiology data, its continued characterization of MC as "likely carcinogenic in humans," based on the mouse lung and liver tumors observed in	EPA added more details about the relevance of mouse data to humans and the fact that metabolites are expected to be the toxic moiety. Upon review of the evidence, EPA considers MC to be "likely carcinogenic in humans." Because 1) metabolites of MC via the GSTT1 pathway are genotoxic; 2) GSTT1 activity is not likely to be completely absent at lower concentrations; and 3) no alternate MOA has adequate support, EPA followed the recommendation of the 2005 *Guidelines for Carcinogen Risk Assessment* (EPA, 2005b) to use linear low dose extrapolation. EPA already discusses uncertainties regarding whether genotoxicity will be observed at lower concentrations (see Section 4.3.5: Key Assumptions and Uncertainties in the Human Health Hazards).

	a high-dose bioassay, is no longer appropriate. • A mutagenic MOA for MC cannot be scientifically justified when there appears to be a kinetic threshold at 500 ppm where genotoxicity (and thus tumors) is unlikely to occur. If the best available science is to be used in the risk evaluation for MC, EPA must take into account the dose-response changes for both the kinetics of MC metabolism and the genotoxicity, which together point to a threshold dose-response being the most appropriate for estimating human cancer risk.	
IUR POD/modeling		
73	**PUBLIC COMMENTS:** • EPA should default to classifying acidophilic and basophilic cell foci from Aiso et al. (2014) as preneoplastic and thus also include them in the Benchmark Dose Software (BMDS) multi-tumor model.	EPA disagrees. Aiso et al. (2014) identified acidophilic and basophilic foci in rats but not mice after chronic inhalation exposure. An oral study also identified altered liver foci (Serota et al., 1986). Because one study identified them in rats and not mice and saw few tumors in rats and because both studies showed that liver foci were not correlated with tumors, EPA considers them most likely to be non-neoplastic.
The IUR calculations are not transparent		
SACC	**SACC COMMENTS:** • The inhalation unit risk values developed for this MC risk evaluation are less protective than previous dose-response assessments by EPA and OSHA, all of which relied on the same underlying data. The risk evaluation should mention this, explain why new inhalation unit risks were derived, and describe exactly how they differ from previous assessments. • In addition, more discussion is needed to support the decision to estimate risk using liver and lung tumors when the calculation of IUR based on mammary tumors gives the	EPA has added more information to explain the difference between the IRIS assessment and the current MC risk evaluation. Because the IUR is based on the lower 95% confidence limit, EPA considered that this adequately covers the risk for the GSTT1 +/+ population and that previous assessments were more conservative than necessary by combining both the GSTT1 +/+ population and the lower 95% confidence limit. EPA has discussed the reasons that the mammary tumors were not used to quantitate risk (See Section 4.3.5).

	highest unit risk. • Recommendation: Add rationale for not using mammary tumors as an endpoint as other evaluations have done.	
73	**PUBLIC COMMENTS:** • Despite the fact that Aiso et al. (2014) identified evidence of carcinogenicity at a lower dose (1000 ppm) than NTP 1986, OPPT (Table 3-20, p. 281) presents calculations suggesting that the IUR based on the NTP study is actually higher than that based on the Aiso et al. (1986) study. EPA must address these apparent inconsistencies as well as explain the details of these crucial calculations much more transparently, as they serve as the basis for its cancer IURs.	Although Aiso et al. (2014) identified carcinogenicity at a lower concentration, the BMD modeling results were nearly identical for both studies resulting in similar IURs. EPA added clarifying language in the dose-response section (Section 3.2.5.2.2). Furthermore, Appendix I includes details regarding the steps used to determine the IUR, and the supplemental file *Methylene Chloride Benchmark Dose and PBPK Modeling Report* (EPA, 2019a) presents more details on the models used.
IUR – Consideration of GST		
73	**PUBLIC COMMENTS:** • EPA's IUR calculation gives insufficient consideration to susceptible subpopulations, because EPA sampled from the "full distribution of GST-T genotypes in the human population". This approach was rejected by EPA in its 2011 IRIS assessment. • EPA should follow the IRIS-recommended approach in its final evaluation and adjust the IUR accordingly. • It should also provide a fuller explanation of all the differences in the IUR calculation in the draft risk evaluation as compared to the 2011 and 2014 IURs and how they impacted the estimates of cancer risk.	EPA did sufficiently consider susceptible subpopulations. EPA has added more information to explain the difference between the IRIS assessment and the current MC risk evaluation. Because the IUR is based on the lower 95% confidence limit, EPA considered that this adequately covers the risk for the GSTT1 +/+ population and that previous assessments (which modeled the GSTT +/+ directly) were more conservative than necessary by combining both the GSTT1 +/+ population and the lower 95% confidence limit. The previous IUR is 75% higher than the updated IUR.
73	**PUBLIC COMMENTS:** • EPA selected the "whole-body GST metric" (i.e., not tissue-specific values) in estimating the combined liver and lung tumor IUR.	The whole-body GST metric is based on a combination of individual liver and lung tissue specific values and is necessary when combining the lung and liver tumors in a single dose-response relationship. This is explained in the risk evaluation (Section

	• There is inadequate explanation for the crucial decision to select the whole-body rather than tissue-specific metric. EPA must provide further details on the scientific rationale for this choice, which directly affects the IUR estimate.	3.2.5.2.2).
IUR does not account for other cancers identified from epidemiological data		
SACC, 55, 75	**SACC COMMENTS:** • Recommendation: Model the dose responses from epidemiological studies and compare these with the dose-response models from the rodent studies to confirm HEC and IUR for chronic and cancer effects, respectively, are sufficiently conservative and health protective. **PUBLIC COMMENTS:** • SACC should recommend to EPA that it quantitatively include the NHL and biliary cancer risks from MC exposure, and other cancer risks, with additional adjustment factors.	Based on the variability in results of the epidemiological studies, EPA determined that the studies are appropriately used qualitatively to support the hazard endpoint in a weight of scientific evidence analysis.
75	**PUBLIC COMMENTS:** • Despite the evidence of breast cancer risks, EPA failed to base the IUR on this endpoint for the following three reasons: (1) only a small number of tumors in animal studies progressed to malignancy; (2) the dose-metric was not certain; and (3) data on mutagenicity in these tissues is lacking. These considerations are inappropriate, unscientific, and inconsistent with EPA's Guidelines.	EPA cited information in the risk evaluation that identified the low conversion from benign to malignant tumors (see Section 4.3.5, Key Assumptions and Uncertainties in the Human Health Hazards). Specifically, with respect to mammary tumors, Russo (2015) indicates that 0.1% of fibroadenomas lead to carcinomas. Therefore, EPA considers our conclusion to be appropriate.
Genotoxicity data		
SACC	**SACC COMMENTS:** • Recommendation: Conduct a data quality evaluation on all in vivo and in vitro	EPA conducted data quality evaluations for all genotoxicity studies and described the results in the risk evaluation (Section 3.2.3.2.1; Appendix K).

	genotoxicity studies included in the MC risk evaluation as described in the application of systematic review in TSCA risk evaluations.	
SACC, 68	**SACC COMMENTS:** • Recommendation: For in vitro genotoxicity studies, provide an in vitro to in vivo exposure extrapolation assessment to estimate equivalent in vivo exposures needed to produce genotoxicity based on in vitro genotoxicity observations. **PUBLIC COMMENTS:** • EPA should consider all possible MOAs using the IPCS/WHO framework and methods to consider confidence in the MOAs (Becker et al. 2017).	EPA acknowledges that this type of extrapolation does have merit. Because there are several *in vivo* genotoxicity studies available for MC, EPA will not consider *in vitro* to *in vivo* extrapolation for MC. EPA has considered multiple modes of action and revised the risk evaluation to include more discussion of multiple MOAs.
Support for mutagenic MOA/linear low dose extrapolation and alternate MOAs		
34, 56, 59, 67, 68, 73	**SACC COMMENTS:** • Recommendation: Include models based on alternative updated MOAs developed by Andersen et al. (2017) and others applying the PBPK model and assumptions within the model, specifically using the internal dose metric of daily mass of MC metabolized into COHb per Andersen et al. (2017) and other alternative MOAs identified by EPA. • Recommendation: Include the alternative updated MOA developed by Andersen et al. (2017) and all other likely mechanisms and, through WOE evaluations, provide the rationale justifying the MOA for MC-induced mouse liver and lung tumors. • The risk evaluation should include dose-response modeling under both the mutagenic and the non-genotoxic mechanisms, and then provide justification for the choice of model used.	Although Andersen et al. (2017) provides an interesting hypothesis regarding a possible MOA, EPA believes that specific mechanisms that might be possible haven't been demonstrated for MC. Furthermore, to EPA's knowledge, an adverse outcome pathway (AOP) describing the molecular initiating and key events hasn't been well established for hypoxia leading to changes in the circadian clock and then subsequently to cancer. For example, EPA found no AOP in development on the AOP wiki (https://aopwiki.org/) or any articles describing relevant MOAs or AOPs in a brief search on PubMed. EPA still considers a mutagenic MOA related to the metabolism of MC by the GSTT1 isoenzyme as having the most support and relevance to human health risk, despite some uncertainties. EPA has added more discussion of these uncertainties to the risk evaluation. Details regarding the MOA suggested by Andersen et al. (2017) include identified changes in gene expression in mice exposed to MC, with marked changes occurring in several genes associated with circadian clocks. Results indicate that liver and lung tumors

	• One Committee member commented on interspecies extrapolation and developing the human-equivalent dose metric and stated the risk evaluation provided no reason for using the default ratio in the model. **PUBLIC COMMENTS:** • Several public commenters representing the HSIA and the American Chemistry Council (ACC) and some SACC members urged EPA to consider a 2017 study by Anderson et al., which uses transcriptomics to evaluate pathways activated in response to MC exposure, arguing it provides evidence for a non-mutagenic cancer MOA. EPA should consider these speculative findings within the context of the extensive and strong evidence base (from epidemiological, in vivo, and in vitro studies) supporting a mutagenic MOA (pp. 245-246). • It is time to reexamine the evidence supporting this genotoxic MOA for MC, especially in light of the toxicogenomic studies and identification of altered oxygen-utilizing pathways and circadian cycle disruption as key events in cancer development. • Risk assessments for MC should focus on elevations in COHb rather than presumptions of a linear, no-threshold risk model based on production of glutathione-pathway metabolites for which there is only limited evidence of mutagenicity in engineered bacterial assays. • At the very least, the present draft TSCA risk	from MC exposure appear to be related to core changes in circadian processes in liver and lung tissue. Andersen et al. (2017) also link circadian rhythms to metabolism showing different patterns in lung versus liver tissue. The common circadian clock effects are for genes that code for regulatory proteins. The authors also identified decreased tissue oxygenation from elevated COHb and the altered association of reduced oxygenation to both circadian cycle proteins and tissue metabolism as the likely mode of action (MOA) for tissue responses to MC, but they note that this conclusion is tentative. In other research, changes in circadian rhythm have been associated with cancer, and some research also links hypoxia to changes in the circadian clock. Iarc (2019) assigned night shift work as Group 2A, probably carcinogenic to humans, based on "limited evidence of cancer in humans, sufficient evidence of cancer in experimental animals, and strong mechanistic evidence in experimental animals." Iarc (2019) also briefly described the mechanistic evidence regarding association between changes in the circadian clock and cancer. Enhanced inflammation was observed in rats. In addition, studies that evaluated changes in light-dark schedules directly measured increased cell proliferation in transplanted tumors. Furthermore, immune suppression was identified in nocturnal rats, mice and Siberian hamsters. Finally, altered tumor glucose metabolism was observed in female nude rats, consistent with the Warburg effect (glucose fermentation in cancer cells). In addition to the link between changes in the circadian clock and cancer, hypoxia has been shown to result in some changes in the circadian clock (Andersen et al., 2017). Some of the mechanistic steps identified in the Iarc (2019) review regarding the induction of tumors via changes in the circadian clock have not been established for MC. In particular, enhanced cell proliferation was either not observed in livers of mice after 78 weeks (Foley et al., 1993) as cited in U.S. EPA (2011), or proliferation from acute and short-term exposure was not sustained after longer (83-93 days) exposure (Casanova et al., 1996; Foster et al., 1992) as

	evaluation for MC should acknowledge the more recent MOA studies – including both toxicogenomic evaluations and improved PBPK models – that cast considerable doubt on the role of short-lived, reactive glutathione pathway metabolites as causative for mouse lung and liver tumors. • EPA should more clearly and transparently present biologically robust, MOA assessments where the weight of the evidence is integrated fully. EPA should carry any biologically plausible alternative MOAs and the default MOA option through the entire assessment and present all risk calculations in the risk characterization section.	cited in U.S. EPA (2011). In addition, although MC has been associated with immunosuppression (Aranyi et al., 1986), EPA has concluded that the evidence is limited. In addition to the MOA suggested by Andersen et al. (2017), no other information was robust enough to consider as a biologically plausible MOA with enough support to carry forward in a comparison with the genotoxic MOA. For interspecies extrapolation to develop the human equivalent concentration, EPA applied a value of $BW^{3/4}$ based on a lack of MC-specific information on the pharmacokinetic differences between laboratory animals (mice and rats for MC) and humans. Use of $BW^{3/4}$ represents our general understanding that metabolic clearance scales allometrically across species. EPA added this reason to Section 3.2.5.2.2 (dose-response for chronic endpoints) of the risk evaluation. The reason is already in Appendix I.
73,75	**PUBLIC COMMENTS:** • Given: (1) existing agency 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 to MC exposure (see, for example, pp. 275, 386), the use of the linear extrapolation is the only appropriate option for cancer dose-response modeling. EPA also must use this approach to cancer dose-response modeling to comply with EPA's duty to consider the "best available science" under TSCA§ 26(h).	Thank you and EPA agrees with this comment.

MC RESPONSE TO COMMENT

EPA should use established framework for alternative MOA evaluation		
68	**PUBLIC COMMENTS:** • EPA should utilize an established framework to organize evidence for MOA based on side-by-side WOE comparison of alternative plausible MOAs (e.g., OECD AOP methodology, WHO/IPCS MOA framework, MOA confidence scores, as described by Becker et al., 2017). Standard MOA templates, such as the dose/temporal concordance and species concordance templates, can be utilized.	EPA evaluated all available evidence, including mechanistic information, related to MOAs and presented the information in Section 3.3.4. EPA considered aspects of the MOA framework (e.g. related to Bradford Hill criteria, whether information was available that indicates key events) when evaluating the available data for methylene chloride.
Route-to-route extrapolation for dermal POD		
SACC	**SACC COMMENTS:** • Recommendation: Add further justification for inhalation-to-dermal extrapolation. • Schenk et al. (2018) recently measured the permeability coefficient and steady-state flux of 38 VOCs, including MC, for newborn pig skin in static diffusion cells.	EPA has added more justification to the use of inhalation data for the route-to-route extrapolation to the dermal route to Section 3.2.5.2.3 (Route to Route Extrapolation for Dermal PODs). Note that the specific information on adjustment for any absorption/permeation is described in the exposure sections. EPA used the permeability coefficient from Schenk et al. (2018) in the dermal calculations.
73	**PUBLIC COMMENTS:** • EPA has made inappropriate assumptions about activity rates in its route-to-route extrapolation for dermal PODs. By assuming only "light activity" in this draft risk evaluation, EPA ignores the potential elevated risk faced by high-activity individuals.	To extrapolate dermal PODs from inhalation PODs, EPA calculated human equivalent doses based on an inhalation rate of 1.25m^3/hr as recommended in EPA's Engineering Manual (cited in an EPA internal document titled *Chemical Engineering Branch Manual for the Preparation of Engineering Assessments*, 1991). That value is based on a standard estimate that the typical worker inhales 10m^3 over the course of an 8 hour workday (Nuclear Regulatory Commission, 2007) and is taken from Niosh (1976). This is the same breathing rate assumption that is used for occupational exposure limits. The daily average value of 1.25m^3/hr is slightly higher than the inhalation rate for light work (1.18m^3/hr) and below the inhalation rate for moderate work (1.75m^3/hr) estimated by NIOSH (1976). Note also that assuming a higher inhalation rate based on moderate

		intensity work for the purposes of route-to-route POD extrapolation would result in a higher POD that may not be appropriate or adequately health protective for all exposure scenarios.
68	**PUBLIC COMMENTS:** • EPA should expand the discussion of the uncertainty associated with the route-to-route extrapolation for dermal hazard evaluation. Several points to clarify in the hazard assessment section could include regulatory precedent, toxicokinetics, route dosimetry and irritation hazard.	EPA has added more information on the uncertainties to Section 4.3, Assumptions and Key Sources of Uncertainty. Due to the dermal contact effects, which include irritation and burns, direct dermal contact with liquid MC should be avoided. Gloves and protective clothing are required in the OSHA standard for workers and when we assume dermal PPE is used, risks to workers are not identified, even with the conservative dermal POD.
75	**PUBLIC COMMENTS:** • Uncertainty relating to the absence of toxicity data for the dermal route of exposure could be considered a "data-base deficiency" warranting an additional UF in determining a benchmark MOE for acute and chronic dermal exposure.	There is no universal list of hazard data required when evaluating chemical risks under TSCA. Furthermore, for methylene chloride, EPA has sufficient, reasonably available hazard information to conduct a risk evaluation and support the use of the chosen hazard endpoints. Therefore, EPA did not use a database uncertainty factor in the methylene chloride risk evaluation.
Consistency with TSCA requirements		
67	**PUBLIC COMMENTS:** • The criteria for interpretation and analysis are policy choices resulting in the regulatory use of an upper confidence limit value calculated using only a selected part of the data. This is not in accordance with TSCA § 26(h) and (i). • The draft risk evaluation's reliance on the 2011 IRIS Assessment is inappropriate in light of the intervening passage of the Lautenberg Act with its requirements that EPA use the best available science and base its decisions on the weight of the scientific evidence. Indeed, the IRIS Assessment used a "strength of the evidence" approach, whereas TSCA § 26(i) expressly requires "decisions under sections 4, 5, and 6 [to be]	EPA used the lower 95th confidence bound of the dose-response to choose a POD to estimate the cancer slope factor for use in the risk evaluation. As suggested by EPAs' 2005 *Guidelines for Carcinogen Risk Assessment* (EPA, 2005b) this lower bound can be used to account for uncertainties in the assessment. EPA considered the use of this lower bound to be appropriate for the current assessment. EPA re-evaluated studies identified in the IRIS assessment and also applied a systematic review process developed specifically for the TSCA risk evaluations, including our own data quality criteria. EPA has added more information to the weight of scientific evidence section to explain EPA's consideration of other possible MOAs, namely the one suggested by Andersen et al. (2017) and thus has based its decisions on the weight of the scientific evidence. EPA disagrees with departing from application of the 2005 *Guidelines for Carcinogen Risk Assessment* (EPA, 2005b) because

	based on the weight of the scientific evidence." • The Guidelines recognize that there may be scientific advances not consistent with the policy-based assumptions and the Guidelines accordingly authorize departure in certain cases from the policy default options. A departure is authorized, indeed necessary, in the case of MC.	no scientific advances that would lead the Agency to depart from the assumptions used have been identified for MC.
Expand toxicokinetics section		
SACC	**SACC COMMENTS:** • Recommendation: Add more explanation to the toxicokinetics section. Pertinent information on interspecies differences in the metabolism and TK of MC needs to be presented (i.e., GST metabolism in the liver, CYP in the lung).	EPA added more summary and comparative information to the toxicokinetics section (Section 3.2.2).
73	**PUBLIC COMMENTS:** • In the discussion of toxicokinetics (Section 3.2.2), EPA has neglected to acknowledge the potential for placental transfer of MC, as documented in the 2011 IRIS assessment.	EPA has added more information on placental transfer to the toxicokinetics section (Section 3.2.2).
Present dose-specific risks for cancer and non-cancer		
73	**PUBLIC COMMENTS:** • EPA should implement the recommendations of the NAS and develop a unified approach to presenting dose-specific population risks for both 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 methylene chloride. These methods include PBPK models for chronic endpoints that use MC-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.
General		

MC RESPONSE TO COMMENT

SACC	**SACC COMMENTS:** • The prediction from Benignus et al. (2011) that the frequency of fatal car accidents may increase at exposures <1 ppm is questionable, and data from other studies included in the risk evaluation could be used to establish a LOAEL of 200-300 ppm. • The risk evaluation misinterpreted the rationale of NAS (2009) in setting its 8-hour AEGL-2 at 60 ppm. • Decrements in performance in humans inhaling up to 751 ppm for 230 minutes were not considered severe enough to significantly impair one's ability to escape a dangerous environment, and thus were not used as the basis of the AEGL-2 derivation. • The values were instead based upon PBPK model simulations of COHb levels at selected exposure times.	The main reason that Benignus et al. (2011) was discussed was to underscore the potential for the association with increased car accidents related to solvent use (which could be a surrogate for workplace accidents); reference to specific concentrations from the study was removed. Reference to the NAS AEGL-2 value in Section 3.2.3.1.1 was removed. AEGL-2 is a level to protect against disabling effects whereas EPA is protecting against effects of lower severity as well. Furthermore, EPA has reviewed all studies and has determined that Putz et al. (1979) can be used to set the POD. See response to commenters # 67, 73 and 45 in the second row in section "Comments on use of ten Berge approach for acute POD"
SACC	**SACC COMMENTS:** • The risk evaluation needs to justify why its analysis approach differs from the EPA's National Center for Environmental Assessment (NCEA) recommendation to use trend tests over pairwise tests.	EPA described the reasons in the supplemental file *Methylene Chloride Benchmark Dose and PBPK Modeling Report*. The endpoints not chosen generally also had unclear dose-response relationships and/or had incidences that noticeably lower than liver and lung tumors.
SACC	**SACC COMMENTS:** • Additional discussion is needed regarding direct vs. indirect (i.e., systemic or blood-based) endpoints due to the acknowledged requirement for metabolism for toxic effect.	See response to commenters # 67, 73 and 45 in the second row in section "Comments on use of ten Berge approach for acute POD"
SACC	**SACC COMMENTS:** • Add more details to Table 3-20 (i.e., spell out what the models are, include how long the simulations were run).	EPA has added more details to Table 3-20
SACC	**SACC COMMENTS:**	EPA added this information to Section 3.2.5.2.1 of the risk

	• p. 274, lines 6275-6278: EPA fails to mention that exercise increases the rates of respiration (alveolar ventilation) and cardiac output, two factors important in increasing systemic uptake of VOCs such as MC.	evaluation.
SACC	**SACC COMMENTS:** • The Agency has not adequately addressed the topic of adverse myocardial effects of VOCs.	EPA added information on cardiac effects in dogs to the hazard identification section on non-cancer effects from acute/short-term exposure (Section 3.2.3.1.1). These studies identify effects (such as cardiac sensitization – ventricular tachycardia or fibrillation and other effects) at 15,000 ppm or higher after very short-term exposures. In answer to the SACC question regarding whether such data are relevant to hypoxia-induced angina, the answer is less clear. COHb levels of 2-4.5% that have been identified as being associated with decreased time to angina are applicable to much lower MC concentrations (< 195 ppm) than the concentrations used in the MC cardiac sensitization studies. EPA considers that the uncertainty factor of 10 for intra-individual variability to account for this effect in individuals with cardiac disease. Use of an uncertainty factor is appropriate to protect the susceptible subpopulation of individuals with cardiac disease and because the direct effects of MC on this population have not been systematically studied.
67	**PUBLIC COMMENTS:** • The draft risk evaluation contains no discussion of scientific issues raised by HSIA and other commenters on both the draft IRIS Assessment and the draft MC Work Plan Assessment released for review in 2014.	EPA responded to comments on the draft IRIS assessment in the final IRIS assessment. EPA also summarized and responded to comments on the draft MC work plan assessment and provided those responses to the public (https://www.epa.gov/sites/production/files/2015-09/documents/dcm_responsetocomments_final.pdf). Finally, EPA has added details to various sections of the current risk evaluation to further elaborate on scientific issues raised by the comments on the current draft risk evaluation.
43	**PUBLIC COMMENTS:** • It would be helpful to have better information	Bornschein et al. (1980) found delayed rates of behavioral habituation to novel environments in offspring from female rats

	on development neurotoxicity in order to determine if the acute PODs based upon adult data are protective of the fetus, infants, and children.	exposed to 4500 ppm MC via inhalation before and/or during gestation. No similar studies with multiple and lower exposure concentrations are available. However, five studies on autism found positive associations with MC (not always statistically significant). For various methodological reasons that include confounding by other chemicals and lack of temporal specificity, EPA did not use these studies in the risk evaluation, but they do identify a neurodevelopmental hazard for humans.
66	**PUBLIC COMMENTS:** • One concern in evaluating this document was a lack of discussion of potential bias of some sourced material. The use and inclusion of corporate sponsored studies could influence how health protective this section and the EPAs recommendations are.	EPA evaluated the merits of the individual studies in the data quality evaluations for each study. The specific metrics within the data quality evaluation domains address several types of biases. EPA considered this approach to be appropriate so that each study, regardless of sponsorship, can be evaluated in a consistent manner.
SACC, 44, 49, 72, 75, 69	**SACC COMMENTS:** • Increase use of the human lethality data. MC has been linked to more than 60 deaths nationwide since 1980 (reference: Safer Chemicals, Healthy Families). One Committee member suggested that the few case reports in Appendix J address this issue insufficiently. **PUBLIC COMMENTS:** • Fatality reports from OSHA and the Massachusetts Department of Public Health are attached to these comments as Exhibit B. • Data from a comprehensive review of 10 sources, all of which are reasonably available to EPA, identified 85 unique deaths related to acute methylene chloride exposure from 1980-2018.	EPA reviewed the sources cited in the SACC and public comments and has updated the text of Appendix J appropriately including reference to the updated compilation of 85 deaths. Note that the same fatalities are often described in multiple data sources. Exhibit B was mentioned in the submitter's comment but was not included as an attachment/available in the docket; therefore, EPA could not review the information.
Editorial		
SACC, 49	**SACC and PUBLIC COMMENTS:** • The SACC and public comments provided many suggestions for editorial comments that	EPA considered and revised many of the editorial suggestions and comments provided by the SACC and the public.

	EPA will consider.	

Risk Characterization
EPA calculated environmental risk using exposure data (e.g. modeling tools and monitored datasets) and environmental toxicity information, accounting for variability within the environment. EPA concludes that methylene chloride poses a hazard to environmental aquatic receptors, with amphibians being the most sensitive taxa identified for aquatic exposures. Risk Quotients (RQs) and the number of days a concentration of concern (COC) was exceeded were used to assess environmental risks. The risk characterization section provides a discussion of the risk and uncertainties around the risk calculations. EPA calculated human health risks for acute and chronic exposures. For non-cancer effects EPA used a margin of exposure (MOE), which is the ratio of the hazard value to the exposure to calculate human health risks. Using an acute non-cancer POD, EPA evaluated potential acute risks for workers for certain scenarios, consumer users and bystanders/non-users (e.g., children, women of childbearing age). A benchmark MOE of 30 was used with the acute POD based on central nervous system (CNS) effects. For chronic occupational risks, EPA used a POD for liver effects as the basis of the chronic non-cancer MOE calculations. A benchmark MOE of 10 was used to interpret chronic risks for workers. An IUR for liver and lung tumors was used to evaluate potential chronic risks to cancer endpoints for the worker exposure scenarios. The risk characterization also provides a discussion of the uncertainties surrounding the risk calculations. **Charge Question 6.1**. Please comment on the characterization of uncertainties and assumptions including whether EPA has presented a clear explanation of underlying assumptions, accurate contextualization of uncertainties and, as appropriate, the probabilities associated with both optimistic and pessimistic projections, including best-case and worst-case scenarios. **Charge Question 6.2**. Please provide information on additional uncertainties and assumptions that EPA has not adequately presented. **Charge Question 6.3**. Please comment on whether the information presented supports the findings outlined in the draft risk characterization section. **Charge Question 6.4**. Please comment on the objectivity of the underlying data used to support the risk characterization and the sensitivity of the agency's conclusions to analytic assumptions made. Risk Characterization: The EPA risk characterization of human health risk from inhalation exposure to workers includes estimates of risk for respirator use. These estimates are calculated by multiplying the high end and central tendency MOE or extra cancer risk estimates without respirator use by the respirator assigned protection factors (APFs) of 25 and 50 (air-supplied respirators). EPA did not assume occupational non users (ONUs) or consumers used personal protective equipment in the risk estimation process. **Charge Question 6.5**. Please comment on whether EPA has adequately, clearly, and appropriately presented the reasoning, approach, assumptions, and uncertainties for characterizing risk to workers using air-supplied respirators and to ONUs and consumers who would not be expected to use PPE.

#	Summary of Comments for Specific Issues Related to Charge Question 6	EPA/OPPT Response
Overall characterization of uncertainties and assumptions		
SACC	**SACC COMMENTS:**	EPA has added language to uncertainties section describing

	• One Committee member stated that there are many lingering uncertainties still pervasive in many aspects of the exposure assessment and the risk characterization. • Recommendation: Add more UFs or better explain the rationale for not doing so.	multiple analyses including for the exposure analysis and risk characterization. EPA considers the current UFs to be sufficient to cover uncertainty and variability in the PODs that have been chosen. EPA added more discussion of the choice of UFs in the risk evaluation.
SACC, 53, 73	**SACC COMMENTS:** • The Committee members observed that increased monitoring efforts (occupational and environmental), coupled with a Bayesian framework could help reduce uncertainty. • Recommendation: Consider following NRC recommendations to use Bayesian UFs in the development of criteria for risk assessment purposes. **PUBLIC COMMENTS:** • There are fundamental flaws in the Simon et al. (2016) implementation of Bayesian/probabilistic methods. A more comprehensive and rigorous framework for probabilistic analysis that already exists in the form of a WHO/IPCS guidance document (WHO/IPCS, 2017b). Other references that can be consulted include Chiu and Slob (2015), Chiu et al. (2018), the APROBA tool on the WHO website, APROBAweb, and the Bayesian Benchmark Dose online web system (benchmarkdose.org). • EPA must provide justification for their decision to deviate from a Bayesian approach.	EPA used reasonably available information for the Risk Evaluation of methylene chloride. In the current risk evaluation, probabilistic models (Monte Carlo analyses) were used in the dose-response models for chronic non-cancer and cancer endpoints. Due to time and resource constraints associated with the deadline for completing the MC Risk Evaluation, EPA cannot implement a Bayesian framework comprehensively for this risk evaluation; however, EPA will consider incorporating more probabilistic modeling into future risk evaluations under TSCA.
66	**PUBLIC COMMENTS:** • It is unclear in some cases why a given UF was chosen, and why a more health protective UF was not used (e.g., Table 4-7; perhaps this was human study, but not explained).	EPA explained the choice of uncertainty factors in Section 3.2.5.2 Derivation of PODs and UFs for Benchmark Margins of Exposures (MOEs). Human data were used for the acute POD.

Interspecies and intraspecies UFs		
SACC	**SACC COMMENTS:** • Several Committee members suggested that UFs should account for differences among people that arise from unknown factors, and not be used to account for differences from known factors, such as GST alleles. One Committee member noted GST variation results in known subpopulations that should be taken into consideration separately, and not considered part of the general intraspecies UF. • The PBPK model does not consider breastfeeding infants (a potentially exposed or susceptible subpopulation), which Committee members suggested may be an issue especially since cited studies have found concentrations of MC in breast milk (Pellizzari et al., 1982). Many felt this is a justification for using an additional or larger UF.	EPA does not use uncertainty factors to account for the GSTT1 +/+ polymorphism in the cancer assessment. Regarding the cancer slope factor, the distribution of GSTT +/+ was modeled using data, and a level of conservatism has already been included in the cancer slope factor by using the lower 95% confidence interval; this was the primary reason that EPA did not add another level of conservatism by basing the risk evaluation only on the GSTT1 +/+ population. Using the 95th confidence interval can be quantitively understood and can also encompass other uncertainties in addition to differences in the presence of the GSTT1 isoenzyme. EPA understands that the GSTT1 polymorphism can also affect individuals' non-cancer responses. For the chronic endpoint of liver toxicity, PBPK modeling relied on metabolites of the CYP2E1 pathway and although the GSTT1 polymorphism may affect the outcome, it is not well understood. For the acute non-cancer CNS endpoint, the GSTT1 polymorphism might influence the amount of CO metabolite available leading to differences in COHb; however, the effect was measured in humans so some GSTT1 distributions should be represented, even given the small sample sizes. Overall, EPA believes that for the non-cancer endpoints, the intraspecies uncertainty factor of 10 is adequate to protect susceptible populations including the GSTT1 polymorphism as well as breastfeeding infants.
45, 49, 55, 44, 72, 75,	**PUBLIC COMMENTS:** • EPA fails to apply certain necessary UFs and departs from its recommended values for others without an adequate explanation. • EPA has identified specific subgroups with biological characteristics that make it likely that they will experience adverse acute effects at lower	In previous assessments (e.g., the new chemicals program), EPA has applied uncertainty factors of 3 instead of 10 when effects are less severe. Furthermore, IRIS assessments have used default uncertainty factors of 3 (EPA, 2002). The risk evaluation states that this value was applied based on the more limited severity of the effect (i.e., the 7% change in just one part of a dual performance task).

	concentrations than healthy adults. To provide protection to these groups, an UF beyond the default intraspecies 10X factor should be applied, as EPA has done for other susceptible groups such as infants and children. An UF of at least 20X, consistent with the EPA Supplemental Cancer Guidance is suggested. • EPA should re-evaluate the approach applied and the appropriateness of assumptions in light of extant occupational assessments that have relied on the same data and reached different conclusions.	EPA used an intraspecies UF of 10 in the risk evaluation, which is expected to protect individuals with cardiac disease that may experience decreased time to angina as well as other susceptible populations. The intraspecies UF was established to account for uncertainty and variability that includes susceptible subpopulations (EPA, 2002). Research indicates that a factor of 10 (when including both toxicokinetics and toxicodynamics) is sufficient in most cases (EPA, 2002), and EPA expects this factor to account for the identified subpopulations applicable to methylene chloride. Occupational assessments may have other goals. For example, OSHA, in their 1997 PEL document, acknowledged that the PEL of 25 ppm considered feasibility of meeting the level and that the PEL was associated with a level resulting in a risk of 3.62 cancer deaths per 1000 population. Furthermore, OSHA notes this level is "clearly well above any plausible upper boundary of the 'significant risk' range defined by the Supreme Court, used by OSHA in its prior rulemakings, and reported in the scientific/economic literature on risk" (OSHA, 1997). In contrast, amended TSCA directs EPA to conduct the risk evaluation without consideration for non-risk factors, such as feasibility of meeting an applicable level.
49, 73, 75, 57	**PUBLIC COMMENTS:** • EPA has failed to justify its deviations from its standard inter- and intra-species UFs. • Reducing the interspecies variability UF is warranted only where there is evidence of correspondence between human and animal response. • EPA guidance likewise cautions against reductions in the 10X UF for intraspecies variability.	For the non-cancer chronic liver endpoint, the portion of the intraspecies uncertainty factor associated with toxicokinetics (3) is not needed because EPA used the 1st percentile of the distribution related to toxicokinetic differences in a PBPK model. Using data derived factors is preferable to applying a default uncertainty factor and EPA expects the use of the 1st percentile to be protective of human health.

		Similarly, the portion of the interspecies uncertainty factor that accounts for toxicokinetic differences between rats and humans was accounted for by the PBPK model.
55	**PUBLIC COMMENTS:** • Because the MC chronic risk estimates are based on liver toxicity, they do not address the risk of neurological effects. It is suggested that EPA use additional adjustment factors to address neurological effects from chronic exposure to MC.	For methylene chloride, EPA has sufficient, reasonably available hazard information to conduct a risk evaluation and support the use of the chosen hazard endpoints.
43, 41	**PUBLIC COMMENTS:** • The SACC should consider why EPA uses the first percentile (HEC99) used for non-cancer effects, particularly since an intraspecies UF of 3 is used. • EPA has not provided adequate evidence to show that variability in sensitivity of specific subpopulations (fetuses, workers and consumers engaged in vigorous activity, individuals with higher CYP2E1 enzyme levels, smokers and individuals with heart disease/cardiac patients) is accommodated by the UFH of 3X. A larger UFH, perhaps 4.5X, should be applied.	EPA used the 1st percentile from the PBPK model to account for variability and uncertainty in *toxicokinetic* differences among humans; this chemical-specific modeled information is preferable to using a default uncertainty factor. However, there may also be toxicodynamic differences among humans. Therefore, EPA considered that an intraspecies UF of 3 is still appropriate, according to guidance and standard practice (EPA, 2002). The commenter does not provide a quantitative reason for suggesting 4.5 vs. 3 as the portion of UF_H to account for toxicodynamic differences among humans. Research indicates that a factor of 10 (when including *both* toxicokinetics and toxicodynamics) is sufficient in most cases (EPA, 2002). Therefore, because the toxicokinetics portion of the UF (rounded to 3) has been accounted for by PBPK modeling, EPA considers that the toxicodynamic UF of 3 is adequate. Furthermore, at least one of the susceptible subpopulations identified by the commenter (individuals with higher CYP2E1) would be accounted for by the use of the 1st percentile from the PBPK modeling. EPA expects that the PBPK modeling and UF of 3 to is sufficient for the identified subpopulations applicable to methylene chloride.
SACC, 73	**SACC COMMENTS:**	There is no universal list of hazard data required when evaluating chemical risks under TSCA. Furthermore, for

	• The Committee questioned why a database UF wasn't included, even if it is not historically used in TSCA evaluations. • Recommendation: Improve the justification for the UFs and/or changes to the UFs and consider including a database UF. **PUBLIC COMMENTS:** • Given potential deficiencies in the study database for MC unrelated to study duration, we assert that the Agency should use a database UF in the MOE derivation. • In addition to identifying toxicity information that is lacking, review of existing data may also suggest that a lower reference value might result if additional data were available. • Consequently, in deciding to apply this factor to account for deficiencies in the available data set and in identifying its magnitude, the assessor should consider both the data lacking and the data available for particular organ systems as well as life stages.	methylene chloride, EPA has sufficient, reasonably available hazard information to conduct a risk evaluation and support the use of the chosen hazard endpoints. Therefore, EPA did not use a database uncertainty factor in the methylene chloride risk evaluation.
49, 73, 75, 55, 43, 44, 72	**PUBLIC COMMENTS:** • EPA acknowledges that it lacks data about immune system, reproductive, and/or developmental endpoints for MC. Moreover, for the endpoint that EPA used to calculate MC's acute risks (neurological effects), EPA acknowledges "uncertainty regarding concentrations and exposure durations that may lead to severe effects and death from inhalation of methylene chloride." • A database UF is further warranted given the potential for hematologic effects (e.g., increased COHb levels), an effect not acknowledged at all in this draft risk evaluation. • The lack of endocrine effects data is another area of data insufficiency for MC.	There is no universal list of hazard data required when evaluating chemical risks under TSCA. Furthermore, for methylene chloride, EPA has sufficient, reasonably available hazard information to conduct a risk evaluation and support the use of the chosen hazard endpoints. Therefore, EPA did not use a database uncertainty factor in the methylene chloride risk evaluation.

	• EPA's final risk evaluation should apply a database UF in determining the benchmark MOE for MC's non-cancer chronic effects.	
43, 73	**PUBLIC COMMENTS:** • EPA needs to apply an UF to account for lack of dermal toxicity data. • EPA's decision to rely on inhalation-to-dermal extrapolation contributes substantial uncertainty to its risk calculations. Therefore, as is recommended for route-to-route extrapolation generally, EPA should apply an additional UF of 10 to account for these uncertainties. • There are concerns about the adequacy of the acute benchmark MOE. EPN would argue that a third UF (UFD) should be incorporated into the derivation of the MOE to accommodate for the incomplete information on neurodevelopment. This third UF could be set at either 1.5X or 2X. The resulting MOE would then be either 45 or 60 (10X (UFH) x 3X (UFL) x 1.5X (UFD) = 45 or (10X (UFH) x 3X (UFL)x 2X (UFD) = 60).	There is no universal list of hazard data required when evaluating chemical risks under TSCA. Furthermore, for methylene chloride, EPA has sufficient, reasonably available hazard information to conduct a risk evaluation and support the use of the chosen hazard endpoints. Therefore, EPA did not use a database uncertainty factor in the methylene chloride risk evaluation. EPA added more discussion of the uncertainty in the inhalation-to-dermal extrapolation in the Key Assumptions and Uncertainties in the Human Health Risk Estimation (Section 4.3.7).
LOAEC-to-NOAEC UF		
SACC, 49, 73, 75	**SACC COMMENTS:** • The selection of a LOAEC-to-NOAEC UF of 3 was not well justified. The reasons for reducing the UF from 10 to 3 based on the magnitude of the effect was unclear, and the Committee noted that other agencies have not done this (e.g., the California OEHHA used 6). One Committee member suggested that a LOAEC-to-NOAEC UF was not needed, since the observed effect (7% decrease) was essentially a NOAEC. **PUBLIC COMMENTS:** • The effects observed in that study are not "of a small magnitude." In addition to a reduction in peripheral vision, which presents serious risks to	In previous assessments (e.g., the new chemicals program), EPA has applied uncertainty factors of 3 instead of 10 for the LOAEC to NOAEC UF when effects are less severe. Furthermore, IRIS assessments have used default uncertainty factors of 3. The risk evaluation states that this value was applied based on the more limited severity of the effect (i.e., the 7% change in just one part of a dual performance task). EPA used an intraspecies UF of 10 in the risk evaluation for effects resulting from acute exposure, which is expected to protect individuals with cardiac disease that may experience decreased time to angina as well as other susceptible populations. The intraspecies UF was established to account for uncertainty and variability that includes susceptible

	many of the commercial and consumer users of MC, the study reported a COHb level in exposed subjects of 5.1%. • The AEGL analysis of MC reports that COHb levels of 4% can lead to "disabling" effects, and EPA's draft risk evaluation states that "at COHb levels of 2 or 4%, patients with coronary artery disease may experience a reduced time until onset of angina (chest pain) during physical exertion." • The LOAEC-to-NOAEC UF of 3 does not seem to be based on any official agency guidance and actually deviates from prior evaluations. An UF of 3 is insufficiently protective of acute inhalation risks.	subpopulations (EPA, 2002). Research indicates that a factor of 10 (when including both toxicokinetics and toxicodynamics) is sufficient in most cases (EPA, 2002). EPA expects this factor to account for the identified subpopulations for methylene chloride.
PPE – general comments		
SACC	**SACC COMMENTS:** • The risk evaluation should highlight those scenarios where safety margins are dependent on proper PPE usage.	EPA outlined its assumptions regarding PPE in section 5.1. Within the unreasonable risk determination for each condition of use, EPA describes assumptions regarding PPE (respirators and gloves), including when use of PPE is not assumed, and the contribution of PPE assumptions to each unreasonable risk determination in section 5.2. EPA has also added a table in Section 4.2.2.1 to make the PPE assumptions made for each occupational exposure scenario clearer. Additionally, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address uncertainty as to whether or not workers are using PPE and using it properly.
SACC	**SACC COMMENTS:** • Emphasis on the insufficient information on appropriate PPE use should be strengthened. It is not clear how lack of knowledge about appropriate use of PPE, or of components in products containing MC (which could synergistically or additively reduce PPE effectiveness) is reflected in the level of confidence on exposures without PPE as compared to PPE use. EPA should be more transparent in this regard.	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. These assumptions incorporate available information on PPE use, including OSHA violation reports and the BLS and NIOSH respirator use surveys.

	• EPA should increase efforts at obtaining specific information on PPE use from users in future risk evaluations. The Agency could reach out to producers and distributors of PPE to determine if they could provide useful information.	EPA's approach for developing exposure assessments for workers is to use reasonably available information and expert judgement to construct exposure scenarios that are anchored in the real-world use of chemicals. 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 judgement underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. 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. EPA will also increase its effort to obtain information on PPE use for future risk evaluations.
SACC	**SACC COMMENTS:** • The Agency's reliance on appropriate use of PPE, including both respirators and gloves, is not supported by current research literature or industrial hygiene practice. • The mere presence of a regulation requiring respirators does not mean that they are used or used effectively. Inadequacies in respirator programs are documented. Respirators require multiple	• 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. These assumptions incorporate available information on PPE use, including OSHA violation reports and the BLS and NIOSH respirator use surveys.

	respiratory protection (RP) compliance factors in order to perform as certified. • Brent et al. (2005) used data from the NIOSH and BLS joint survey on Respirator Usage in Private Sector Firms (BLS, 2001) to examine the adequacy of respirator protection programs in private industries. They found "large percentages of establishments requiring respirator use [under OSHA or the Mine Safety and Health Administration (MSHA) regulations] had indicators of potentially inadequate respirator programs." Later, Janssen et al. (2014) reported that "APFs do not apply to RPD used in the absence of a fully compliant RP program; less than the expected level of protection is anticipated in these situations." • The frequency of *proper* use of gloves and respirators is largely unknown. • There is variability in use of PPE across manufacturing facilities, with larger and better-funded manufacturing industries and facilities often having industrial hygiene compliance programs. • The Committee encouraged EPA to look for existing literature on PPE use and recommends that EPA consider OSHA violation reports on glove and respirator use which may provide data on the frequency or extent of usage in the industry. • The Committee suggested that the NIOSH BLS respirator usage survey can be used to provide industry-based estimates of respirator program effectiveness, which could then be employed to set the best APF for an industry. • One Committee member indicated that the high-end exposure scenarios do not include PFs derived from assumed respirator use.	• EPA's approach for developing exposure assessments for workers is to use reasonably available information and expert judgement to construct exposure scenarios that are anchored in the real-world use of chemicals. 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 judgement underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. 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.
73	**PUBLIC COMMENTS:**	EPA's approach for developing exposure assessments for workers is to use the reasonably available information to

	• EPA has adopted a flawed assumption – absent any empirical evidence to support it – that workers under many conditions of use of MC will always wear effective PPE, including gloves.	construct exposure scenarios that are anchored in the real-world use of chemicals. 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. 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 MC, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE. EPA's assumption that workers are typically protected by PPE is based on consideration of the OSHA regulations at 29 CFR 1910.1052, which sets the methylene chloride standard, including which circumstances necessitate the use of personal protective equipment (PPE). Thus, 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.
66	**PUBLIC COMMENTS:** • Draft risk evaluation (line 8109): what type of gloves are being used? Some materials amplify the dermal exposure from gloves; verify with the glove standard.	Protective gloves in this table are either PF5, PF10, or PF20. Use of PF > 1 means that the gloves are protective and have permeation data to support the greater protection factor and possibly various levels of training. Gloves that are not protective have PF = 1.

52	**PUBLIC COMMENTS:** • From p. 181; For consumer usage, it is expected that proper PPE is rarely worn with the exception of gloves for dermal exposure (still expect low usage of PPE). I do not know how best to comment on the data in Tables 2-94 and 2-95 other than the concern for lack of PPE being used.	Modeled consumer exposures (both inhalation and dermal) are evaluated based on the reasonable assumption that consumers and bystanders would not be wearing PPE.
52	**PUBLIC COMMENTS:** • From p. 319; Focus on the data from the "No Respirator" values as this is more in line with usage that is observed in practice.	EPA's approach for developing exposure assessments for workers is to use the reasonably available information to construct exposure scenarios that are anchored in the real-world use of chemicals. 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. 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 MC, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE. EPA's assumption that workers are typically protected by PPE is based on consideration of the OSHA regulations at 29 CFR 1910.1052, which sets the methylene chloride standard, including which circumstances necessitate the use of personal protective equipment (PPE). Thus, 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.
69	**PUBLIC COMMENTS:** • EPA continues to inappropriately assume that workers wear both respirators and protective gloves in its risk calculations. • "Based on the protection standards, inhalation exposures may be reduced by a factor of 25, 50, 1,000, or 10,000, if respirators are required and properly worn and fitted."	EPA's approach for developing exposure assessments for workers is to use the reasonably available information to construct exposure scenarios that are anchored in the real-world use of chemicals. 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 MC, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE. EPA's assumption that workers are typically protected by PPE is based on consideration of the OSHA regulations at 29 CFR 1910.1052, which sets the methylene chloride standard, including which circumstances necessitate the use of personal protective equipment (PPE). Thus, 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.
73, 66	**PUBLIC COMMENTS:** • EPA makes clear that its risk determinations "incorporate consideration of expected PPE (frequently estimated to be a respirator of APF 25 or 50 and gloves with PF 5-20)" (p. 33). • Given the types of respirators used to be able to achieve an APF 25 or 50, a more protective consideration would be to lower the limit rather than rely on personal protective equipment. • Line 8117: for gloves with PFs of 10 not being protective enough, levels should be lowered.	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. 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.
PPE assumptions – respirator use		
SACC, 49, 73, 57, 43, 44, 72, 75,	**SACC COMMENTS:** • Several Committee members questioned the use of APFs to indicate protectiveness of PPE, and others noted that the actual use of PPE as well as the proper use of PPE in affected occupations had not been sufficiently investigated. **PUBLIC COMMENTS:** • EPA assumes that workers wear respirators and protective gloves for the entirety of their work shift, every day throughout their careers. • Because TSCA requires risk management only after EPA has made an unreasonable risk determination, and only to the extent needed to address the risks that EPA has found unreasonable, EPA's PPE assumptions leave millions of workers unprotected or under-protected.	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. 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.
72, 73, 42, 63	**PUBLIC COMMENTS:** • EPA incorrectly assumes that all workers in many conditions of use will be provided and will use PPE, without any supporting evidence. Even within a	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

	given condition of use (e.g., the commercial use of lubricants and greases containing MC), there often are a wide range of employers and workplaces. • EPA should more clearly specify precisely which conditions of use workers are presumed to wear PPE and how it determined whether workers exposed from a given condition of use were expected to use PPE.	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 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.
SACC, 49, 73, 72, 75, 33, 77	**SACC COMMENTS:** • The assumptions and uncertainties with regard to respirator use and the assumed protection are not discussed in Sections 4.3.2 and 4.3.7. • Recommendation: Discuss more thoroughly all the assumptions made with respect to respirator use and its protective effect. **PUBLIC COMMENTS:** • EPA made it clear that it does not have any actual data on respirators or gloves, such as types used and frequency. EPA assumed without evidence various levels of protection from different purely hypothetical PPE scenarios. • EPA's risk evaluations must be supported by "substantial evidence" in the administrative record. Not only do EPA's unsupported assumptions of PPE use fall far short of that standard, but in many instances, they are directly contrary to EPA's prior findings and analyses.	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 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.
SACC, 49, 73, 42, 44, 72, 75, 63, 77, 83	**SACC COMMENTS:** • The Committee expressed concern that long-term repeated inhalation exposures to MC can lead to other respiratory illnesses, such as asthma, which	EPA has not identified reasonably available information associating asthma with MC. EPA's approach for developing exposure assessments for

	has been reported with long-term exposures to VOCs in general. • Discussion of PPE use in the risk evaluation did not address known factors that affect workers' or ONUs' use of PPE, such as discomfort, limitations in movement, sensory perception (i.e., hearing, vision, touch). These factors are exacerbated as task-time and temperature increase, implying that even under the best-case scenario of proper use of PPE at the beginning of a work shift, use of PPE will degrade over time, both within a daily work shift and over the course of a worker's career because of increasing reluctance to use PPE. **PUBLIC COMMENTS:** • EPA's PPE assumptions are also contrary to EPA's prior findings concerning MC (January 2017 proposal to ban consumer and commercial uses of MC paint strippers). Individuals with impaired lung function due to asthma, emphysema, or chronic obstructive pulmonary disease, for example, may be physically unable to wear a respirator. • There are clear differences in the size and sophistication of employers, workplace demographics and language barriers, and working conditions that may make PPE more burdensome, if not prohibitive. • OSHA and NIOSH have similarly found that respirators can cause discomfort, skin irritation, heat stress, communication difficulties, and vision limitations, and that they often create other hazards for workers, such as trips, falls, and "struck by" hazards. • The increased heat hazard associated with respirator use is a significant limitation of the draft risk evaluation, given that many users of MC are likely to work outside or in non-air-conditioned spaces.	workers is to use the reasonably available information to construct exposure scenarios that are anchored in the real-world use of chemicals. 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. The OSHA regulations at 29 CFR 1910.1052 set forth the methylene chloride standard, including which circumstances necessitate the use of personal protective equipment (PPE). Thus, 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.

	Moreover, with warming conditions globally due to climate change, it is "reasonably foreseen" that PPE which imposes additional heat stress will be even less frequently used. • The 2017 proposal also recognized that effective use of PPE requires clear and understandable hazard warnings and directions for safe use together with adequate employee training and oversight. Absent such warnings and a requirement that workers use approved PPE when handling MC, EPA's assumption that workers are using the "expected" PPE is likely false.	
52	**PUBLIC COMMENTS:** • Our experience is that engineering controls can be too expensive for commercial shops to install and proper PPE is often, if not usually, not worn.	EPA's approach for developing exposure assessments for workers is to use the reasonably available information to construct exposure scenarios that are anchored in the real-world use of chemicals. 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 MC, EPA has determined that

		most conditions of use pose an unreasonable risk to workers even with the assumed PPE. The OSHA regulations at 29 CFR 1910.1052 set forth the methylene chloride standard, including which circumstances necessitate the use of personal protective equipment (PPE). Thus, 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.
63, 70, 75, 77	**PUBLIC COMMENTS:** • It should be noted that many of the subcategories in Table 4-104 (p. 395) involve multi-task cleaning and repair operations that may require close worker examination of treated metals and materials, which may not be possible with the types of respirators permitted for MC. • The Massachusetts TURA program staff have observed workers using MC without appropriate PPE. • It is very likely that smaller establishments and family owned businesses (e.g., dry cleaners) will not likely use or properly utilize PPE (ie., Blando et al., 2010; CDC, 2008).	EPA's approach for developing exposure assessments for workers is to use the reasonably available information to construct exposure scenarios that are anchored in the real-world use of chemicals. 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 MC, EPA has determined that most conditions

		of use pose an unreasonable risk to workers even with the assumed PPE. The OSHA regulations at 29 CFR 1910.1052 set forth the methylene chloride standard, including which circumstances necessitate the use of personal protective equipment (PPE). Thus, 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.
73, 66	**PUBLIC COMMENTS:** • Organic solvents like MC may breakthrough the carbon or other medium in organic vapor cartridge respirators, and this can occur without providing any indication to the user that the respirator is no longer functioning. • EPA has acknowledged ensuring protection necessitates use of air-supplied respirators.	Thank you for your comment.
73, 66, 44, 72, 75, 63	**PUBLIC COMMENTS:** • EPA's deviation from the hierarchy of controls violates the obligation to use the best available science in TSCA risk evaluations. • The hierarchy of controls should be followed to eliminate workplace hazards. PPE has the highest failure rate and is the least effective control, since it does not eliminate the hazard and is subject to human error. OSHA and NIOSH manage chemical risks using the "hierarchy of controls." • NIOSH states the following regarding PPE: "PPE (e.g., respirators, gloves, protective clothing) is the least desired option for controlling worker exposures to hazardous substances. PPE is used when engineering and administrative controls are not feasible or effective in reducing exposures to acceptable levels or while controls are being	OSHA's 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 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. Rather, these risk estimates are part of EPA's approach for developing exposure assessments for

	implemented. It is the last line of defense after engineering controls, work practices, and administrative controls." • OSHA has also highlighted the major limitations of reliance on PPE. In 2016, OSHA informed EPA that respirators are the "least satisfactory approach to exposure control," stating that respirator effectiveness ultimately relies on the practices of individual workers who must wear them. EPA affirmed its agreement with OSHA's conclusions in its proposed TSCA Section 6 rule to ban MC-based paint strippers in both consumer and commercial settings.	workers that use the reasonably available information to construct exposure scenarios that are anchored in the real-world use of chemicals. 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., 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), 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 MC, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE. EPA's assumption that workers are typically protected by PPE is based on consideration of the OSHA regulations at 29 CFR 1910.1052, which sets the methylene chloride standard, including which circumstances necessitate the use of personal protective equipment (PPE). Thus, 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.
PPE assumptions - gloves		
SACC	**SACC COMMENTS:** • Committee members were unclear as to how PPE use is factored into the human health risk calculations (e.g., MC can penetrate gloves necessitating frequent changing of gloves). • Recommendations: Add the use of respirator and personal gloves as both a key assumption and as a source of uncertainty. And acknowledge that workers do not wear gloves continuously over their work shift and incorporate this assumption into calculations of risk for certain categories of workers.	EPA added a table in Section 4.2.2.1 to make the PPE assumptions made for each COU clearer. EPA has also 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. Additionally, Section 4.3.2.3 Occupational Dermal Exposure Dose Estimates mentions glove protection factors, based on the ECETOC TRA model as described in Section 2.4.1.1, are "what-if" assumptions and are uncertain. EPA does not know the actual frequency, type, and effectiveness of glove use in specific workplaces of the OESs.
SACC	**SACC COMMENTS:** • Regarding the statement in the risk evaluation, "Initial literature review suggests that there is unlikely to be sufficient data to justify a specific probability distribution for effective glove use for a chemical or industry" (p. 110, lines 1918-1922), the EPA should present and/or reference the literature reviewed and should be clear when they believe that PPE will be used within an industry and present the appropriate justification. The EPA should indicate when/if the assessment of PPE use was made based on professional judgment.	EPA added a table in Section 4.2.2.1 to make the PPE assumptions made for each COU clearer.
73, 44, 72, 75, 70, 74	**PUBLIC COMMENTS:** • EPA acknowledges that protection varies greatly with different glove materials; however, the agency cites no data on actual use of specific glove types, and instead simply assumes default glove PFs. • EPA indicated that it does not have any actual data on gloves, such as the types used and frequency, or	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

	data on the proper use of effective gloves in industrial settings. • OSHA makes specific recommendations about MC-resistant gloves. TURA program staff have observed workers using non-recommended gloves in some cases. At a furniture refinishing facility, TURA program staff did observe the use of more protective, multiple-layer laminate gloves; however, the same pair of gloves was used over a long period of time. TURA program staff have observed that many workers are unfamiliar with the concepts of breakthrough and degradation time for gloves.	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. EPA's assumption that workers are typically protected by PPE is based on consideration of the OSHA regulations at 29 CFR 1910.1052, which sets the methylene chloride standard, including which circumstances necessitate the use of personal protective equipment (PPE). Thus, 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. Regarding the comment about TURA program staff observing in some instances that there is proper glove use while not at other times, because EPA uses the high-end exposure values to account for uncertainties and variabilities in PPE usage, this is accounted for in its unreasonable risk determinations.
49, 72, 70, 73	**PUBLIC COMMENTS:** • Improper glove use can lead to increased worker exposures due to "contamination of the interior of the glove" (if workers are not properly training in glove use and replacement) or by "acting as a reservoir" for contaminants (if the gloves are not impermeable). • Notably, "EPA has not found information that would indicate specific activity training (e.g., procedure for glove removal and disposal) for tasks where dermal exposure can be expected to occur in a majority of sites …" • TURA program staff have observed that MC users do not necessarily use gloves when handling the	EPA's approach for developing exposure assessments for workers is to use the reasonably available information to construct exposure scenarios that are anchored in the real-world use of chemicals. 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

	chemical; users also lack information on correct choice of gloves, and even sometimes re-use contaminated gloves. • EPA must therefore consider the foreseeable exposure scenarios in which employees are not provided protective gloves, or, worse, are provided inadequate gloves or are not adequately trained and thus face even greater dermal exposures due to glove contamination and the occlusion of MC close to the skin.	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 MC, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE. EPA's assumption that workers are typically protected by PPE is based on consideration of the OSHA regulations at 29 CFR 1910.1052, which set the methylene chloride standard, including which circumstances necessitate the use of personal protective equipment (PPE). Thus, 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. Regarding the comment about TURA program staff observing in some instances that there is proper glove use while not at other times, because EPA uses the high-end exposure values to account for uncertainties and variabilities in PPE usage, this is accounted for in its unreasonable risk determinations.
SACC, 73	**SACC COMMENTS:** • The Committee recommends that for high-end exposure scenarios where workers are expected to be exposed for longer duration at higher chemical	EPA's approach for developing exposure assessments for workers is to use the reasonably available information to construct exposure scenarios that are anchored in the real-world use of chemicals. As stated in section 5.1.1.3, EPA

	concentrations, the glove PF should be limited to five or one, regardless of industry. **PUBLIC COMMENTS:** • EPA appears to want to have it both ways: To acknowledge the limitations of gloves and their potential to increase skin absorption, but then to simply assume that gloves actually provide 5x, 10x, or 20x levels of protection over no gloves – regardless of the potential for occlusion – without citing any evidence to support these values. • This approach will allow clear risks to occur whenever a worker uses anything less than the most protective gloves (or no gloves), or when there is occlusion; these scenarios are quite likely – and certainly reasonably foreseen – to occur in the real world.	assumes the use of gloves with PF of 5 and 10 in commercial settings and gloves with PF of 5 and 20 in industrial settings. For the exposure scenarios referenced by the Committee, EPA determined it is appropriated to assume glove PFs of 5, 10, 02 20 (with specific assumptions described in the unreasonable risk determination for each condition of use, in Section 5.2). EPA does not factor in duration of dermal exposure in the occupational exposure scenarios because the durational of dermal exposure for different occupational exposure activities across various workplaces are often not known (see Section 2.4.1.1). While EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. Once EPA has applied the appropriate PPE assumption for a particular condition of use in each unreasonable risk determination, in those instances when EPA assumes PPE is used, EPA also assumes that the PPE is used in a manner that achieves the stated APF or PF. EPA agrees that there are challenges to achieving full protection from PPE. 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.
73	**PUBLIC COMMENTS:** • Gloves can also increase skin temperature and humidity, which can increase absorption. Therefore, the assumption that PFs can only range as low as 1x (no gloves) is erroneous; rather, the range should include PFs below 1x.	EPA's assumptions and methodology for estimating dermal risks are described in section 2.4.1.1, including assumptions about glove use and associated protection factors. The data about the frequency of effective glove use – that is, the proper use of effective gloves – is very limited in industrial settings. Initial literature review suggests that there is unlikely to be sufficient data to justify a specific probability distribution for effective glove use for a chemical or industry. Instead, the impact of effective glove use is explored by considering different percentages of effectiveness. EPA also considered potential dermal

		exposure in cases where exposure is occluded. See further discussion on occlusion in Appendix E of the Supplemental Information on Releases and Occupational Exposure Assessment document.
OSHA – assumptions and regulations		
49, 72, 75, 63	**PUBLIC COMMENTS:** • EPA misrepresents OSHA regulations with respect to the use of PPE. 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." • With respect to MC, OSHA's regulators expressly require employee exposures and risks to be measured without the use of respiratory protection. OSHA permits the use of respirators only if "engineering controls and work practices" cannot achieve OSHA's PEL on their own.	EPA's approach for developing exposure assessments for workers is to use the reasonably available information to construct exposure scenarios that are anchored in the real-world use of chemicals. 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., 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), 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 MC, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the

		assumed PPE. EPA's assumption that workers are typically protected by PPE is based on consideration of the OSHA regulations at 29 CFR 1910.1052, which sets the methylene chloride standard, including which circumstances necessitate the use of personal protective equipment (PPE). Thus, 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.
73, 49, 69	**PUBLIC COMMENTS:** • OSHA's database of inspections demonstrates significant noncompliance with OSHA respiratory protection requirements (e.g., 2,892 violations of the respiratory protection standard identified in 1,281 separate inspections in 2018). • EPA thus has no basis for assuming that employers will voluntarily exceed OSHA requirements and provide respirators even in circumstances where it is not required.	OSHA data are collected as part of compliance inspections at carious types of facilities. Certain industries are typically targeted based on national and regional emphasis programs. Other inspections may be prompted based on complaints or referrals. As a result, OSHA data may underrepresent PPE usage throughout the affected industry. Additionally, because EPA uses the high-end exposure values to account for uncertainties and variabilities in PPE usage, this is accounted for in its unreasonable risk determinations. EPA's approach for developing exposure assessments for workers is to use the reasonably available information to construct exposure scenarios that are anchored in the real-world use of chemicals. 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., 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), 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 MC, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE. EPA's assumption that workers are typically protected by PPE is based on consideration of the OSHA regulations at 29 CFR 1910.1052, which sets the methylene chloride standard, including which circumstances necessitate the use of personal protective equipment (PPE). Thus, 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.
72	**PUBLIC COMMENTS:** • OSHA has recognized atmosphere-supplying respirators are a relatively expensive type of respiratory equipment, requiring the employer not only to purchase the respirators themselves but also to install an air compressor and associated ductwork or rent cylinders containing breathing air.	Thank you for your comment. 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

	• In the case of MC, the situation is complicated by the predominance of relatively small companies among the employers whose employees are currently exposed above the 8-hour TWA PEL.	uncertainties and variabilities in PPE usage (e.g., 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), 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.
42	**PUBLIC COMMENTS:** • To fully evaluate EPAs assumptions regarding PPE use, EPA should provide any feedback it has received from OSHA and NIOSH on its assumption regarding PPE use, and more generally, any input they have provided EPA regarding the extent and sufficiency of OSHA's authorities.	EPA does not share internal deliberative comments from the interagency review process. However, other agencies can make their comments public by submitting their comments to the docket.
73, 75, 69, 11, 49, 66, 72	**PUBLIC COMMENTS:** • EPA inappropriately invokes the OSHA PEL as a benchmark. The OSHA PEL for MC is not health-protective and EPA identified unreasonable risks at concentrations five times below the PEL (i.e., chronic liver toxicity at <5 ppm). OSHA calculated a cancer risk of 3.62 deaths per 1,000 workers exposed to the PEL over a working lifetime, a level of risk several times above that which EPA deems acceptable. • In the 2017 proposed ruling, EPA developed a recommendation for an ECEL as a more current benchmark for workplace exposures (1.3 ppm 8-hour TWA). Under the manufacturing condition of use, the high-end 8-hour TWA exposure concentration (4.6 mg/m3 or 1.32 ppm) would just exceed the ECEL of 1.3 ppm.	In Chapter 2, exposures were compared to the PEL because exposures above the PEL would require mitigation under the OSHA standard. 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. EPA did not recommend this ECEL in the 2017 proposed rule for MC in paint and coating removal (82 FR 7464, January 19, 2017). Rather, the ECEL was one possible risk management approach outlined in the rulemaking that proposed to prohibit the use of methylene chloride in most commercial paint and coating removal. This ECEL was not finalized and thus, there is no ECEL for methylene chloride.

65	• The de minimis occupational cancer risk policy levels between OSHA and EPA differ by one order-of- magnitude, exactly as does the OSHA PEL when converted using the EPA IUR. This means that at the PEL, EPA's "no unreasonable risk" criteria are met for cancer endpoint (and for non-cancer endpoints, for which EPA's risk levels are only exceeded at higher exposures). Thus, no unreasonable risk exists in OSHA-compliant manufacturing facilities.	As noted in the draft risk evaluation, EPA relied on NIOSH guidance when choosing the 10^{-4} cancer risk benchmark to evaluate risks to workers from methylene chloride exposure. Furthermore, OSHA, in their 1997 PEL document, acknowledged that the PEL of 25 ppm considered feasibility of meeting the level and that the PEL was associated with a level resulting in a risk of 3.62 cancer deaths per 1000 population. OSHA notes this level is "clearly well above any plausible upper boundary of the 'significant risk' range defined by the Supreme Court, used by OSHA in its prior rulemakings, and reported in the scientific/economic literature on risk." (OSHA, 1997). In contrast, TSCA compels EPA to evaluate chemicals without consideration of non-risk factors (such as feasibility of meeting a standard) to determine whether they present unreasonable risk under the conditions of use. EPA's "no unreasonable risk" standard has not necessarily been met at the PEL.
68	**PUBLIC COMMENTS:** • To satisfy Section 9's coordination requirements, as well as TSCA's call for increased transparency in decision-making, EPA should provide more information about how it determines whether existing regulations under other statutes are adequate to address potential risks associated with a TSCA chemical under certain conditions of use.	As part of the problem formulation for methylene chloride, EPA identified exposure pathways under other environmental statutes administered by EPA, i.e., the Clean Air Act (CAA), the Safe 9892 Drinking Water Act (SDWA), the Clean Water Act (CWA) and the Resource 9893 Conservation and Recovery Act (RCRA). The Office of Chemical Safety and Pollution Prevention works closely with EPA offices that administer and implement the regulatory programs under these statutes. EPA believes that the TSCA risk evaluation should focus on those exposure pathways associated with TSCA uses that are not subject to the regulatory regimes discussed above because these pathways are likely to represent the greatest areas of concern to EPA. Clarifying language about what pathways are addressed under other statutes has been added to Section 1.4.2 of the Risk Evaluation.

The impact of PPE assumptions on risk determination		
SACC, 57, 43, 72, 73, 44, 69	**SACC COMMENTS:** • One Committee member thought that PPE use should not be considered when determining risk. Rather, it should be considered only in a risk management phase, except for conditions of use where EPA ascertains the proper use of PPE and other exposure controls at least 95% of the time. • EPA should consider any scenarios that present unreasonable risks without assuming PPE use, while the risk management process should be focused on designing and ensuring appropriate PPE use and other controls. **PUBLIC COMMENTS:** • While EPA may assess and characterize worker risk with and without the use of PPE, it should make its unreasonable risk determinations based upon the "no PPE" scenarios. Lacking the guarantee of consistent use of PPE, EPA should focus its regulatory options on mitigating risk to the unprotected individual. • By assuming extensive use of PPE at the risk evaluation stage, EPA conflates risk evaluation with risk management and preempts the required consideration of alternate regulatory tools during the risk management stage, in violation of TSCA. • PPE assumptions are the key driver of a large fraction of EPA's inhalation risk determinations for workers – both in cases where EPA did find unreasonable risk and in cases where it did not. If EPA's PPE assumptions erase unreasonable risks, then EPA will not regulate the chemical under TSCA and will forgo its only opportunity to ensure that PPE is actually used and workers are protected.	For the purposes of unreasonable risk determinations, EPA is assuming the use of PPE on a case-by-case basis for each COU and how it is used (i.e., industrial, commercial, consumer) in contrast to the approach EPA would take in any regulatory action, which is to eliminate workplace hazards by requiring certain actions occur to address the unreasonable risk. EPA's approach for developing exposure assessments for workers is to use the reasonably available information to construct exposure scenarios that are anchored in the real-world use of chemicals. 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 MC, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE.

		EPA's assumption that workers are typically protected by PPE is based on consideration of the OSHA regulations at 29 CFR 1910.1052, which sets the methylene chloride standard, including which circumstances necessitate the use of personal protective equipment (PPE). Thus, 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.
SACC	**SACC COMMENTS:** • Some Committee members appreciated that Table 4-104 presented an evaluation of human health risk without the use of PPE and its reduction due to PPE use, and found the table to be effective in communicating results. • Other Committee members felt that the table was too detailed to navigate easily. One suggestion was that the Table show results only for three categories: no unreasonable risk, no unreasonable risk under condition of proper PPE use, and unreasonable risk even under conditions of proper PPE use.	Table 4-104 provides information to summarize the risk characterization, not the unreasonable risk determination. The format of this table and the unreasonable risk determination have both been updated for greater clarity.
73	**PUBLIC COMMENTS:** • EPA finds no unreasonable risk for acute (15-minute) non-cancer effects from inhalation during processing of MC as a reactant – despite the fact that its MOE is substantially lower than its benchmark MOE (4.9 and 30, respectively); it does so only by assuming universal and effective use of a respirator with an APF of 25 (see Table 4-9, p. 307).	Based on the OSHA standard for methylene chloride at 29 CFR 1910.1052, the only respirators that can be considered by EPA are supplied-air respirators (i.e., APF of 25 would be the lowest APF that could be considered), further discussed in section 2.4.1.1. Therefore, for each condition of use of methylene chloride with an identified risk for workers, EPA assumes, as a baseline, the use of a respirator with an APF of 25 or 50. 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.
75	**PUBLIC COMMENTS** • EPA calculates cancer risks above its "benchmark" of 1 x 10^{-4} for several workplace exposure scenarios in the absence of respirators and gloves but then determines that use of PPE would lower the risk below the benchmark. If finalized, EPA's determinations of no unreasonable risk would mean that these workers receive no protection against cancer risk under Section 6(a) of TSCA. • EPA uses the same approach in assessing non-cancer risks to workers. Numerous worker categories have highly unprotective MOEs in the absence of PPE but would be adequately protected if PPE is used. As a result, workers at risk of serious acute and non-cancer chronic effects (including death and severe incapacitation) would receive no protection under Section 6(a) based on the unrealistic "expectation" that use of PPE would prevent harm. • EPA's approach is not grounded in data, departs from established workplace protection policy and is contrary to the realities of worker exposure to unsafe chemicals.	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. Such consideration carries extra importance when the risk estimates are close to the benchmarks for acute, chronic non-cancer risks, and cancer risks. EPA's approach for developing exposure assessments for workers is to use reasonably available information and expert judgement to construct exposure scenarios that are anchored in the real-world use of chemicals. 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 judgement underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. 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. 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.
73	**PUBLIC COMMENTS:** • For each of the 29 conditions of use where EPA assumed routine use of respirators, EPA's assumption of respiratory PPE use "eliminated" or "understated" 74% of the risk estimates calculated for the conditions of use. • Of the 29 conditions of use, EPA made a final risk determination that 19 of them presented unreasonable risk to workers, while 10 did not. • In at least the 19 cases just noted, EPA took the wholly unjustifiable approach of finding a risk to be unreasonable only if the risk from both the high-end and the central tendency exposures exceeded its acceptable risk levels. In contrast, in its draft risk evaluation for 1-BP, EPA took the far more justifiable approach of finding a risk to be unreasonable even when the risks from only the high-end exposure exceed its acceptable risk levels. That approach is necessary to ensure that those experiencing high-end, i.e., sentinel, exposures will always be protected. For EPA not to do so would be inconsistent with its own definition of sentinel exposure in the risk evaluation rule. See 40 CFR § 702.33.	EPA examines the totality of risk estimates for a condition of use when making a determination of unreasonable risk. EPA makes one determination for each condition of use and describes the basis in terms of risks to workers and ONUs, with specificity to what kind of risks. For worker exposures, for the purposes of determining whether 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 MC, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE. Regarding the use of central tendency and high-end risk estimates, in the draft and final risk evaluations for methylene chloride, EPA used the high-end exposure value when considering worker risks in order to address the uncertainties and variability in PPE usage. In both the draft and final risk evaluations, EPA used the central tendency exposure value when considering ONU exposures when the data did not distinguish between worker and ONU exposures.

		EPA assumed that all ONU exposures should not be presented as identical to exposures of workers directly handling or using the chemical. EPA has, where possible, estimated far-field ONU exposures and described the risks separately. To account for those instances where monitoring data or modeling did not distinguish between worker and far-field ONU inhalation exposure estimates, EPA considered the worker central tendency risk estimate when determining far-field ONU risk.
73, 70	**PUBLIC COMMENTS:** • For every occupational exposure scenario EPA examined, EPA found no unreasonable risk from dermal exposure only by assuming that workers wear gloves delivering a level of protection sufficient to protect against dermal exposures (examples were provided). • For all 23 scenarios, EPA found that the exposures, absent glove use, present unreasonable risks for both acute and chronic, non-cancer health effects. EPA then assumed that all workers under all those scenarios would routinely wear the right gloves that always provided effective dermal protection and never led to situations of chemical breakthrough or occluded exposures. • Through this assumption, EPA effectively eliminated from consideration all of its no-glove risk estimates, each of which yielded an MOE falling below EPA's benchmarks MOEs, indicating unreasonable risk.	Based on the OSHA standard for methylene chloride at 29 CFR 1910.1052, the only respirators that can be considered by EPA are supplied-air respirators (i.e., APF of 25 would be the lowest APF that could be considered), further discussed in section 2.4.1.1. Therefore, for each condition of use of methylene chloride with an identified risk for workers, EPA assumes, as a baseline, the use of a respirator with an APF of 25 or 50. Similarly, EPA assumes the use of gloves with PF of 5 and 10 in commercial settings and gloves with PF of 5 and 20 in industrial settings. 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.
51	**PUBLIC COMMENTS:** • We request that EPA revise Section 4.2.2.1.20 – and all risk estimates and conclusions derived in or	While use of methylene chloride as a functional fluid in a closed system during pharmaceutical manufacturing was included in the problem formulation and draft risk evaluation, upon further analysis of the details of this

	from that section – to reflect pharmaceutical manufacturers actual current practices. • JMI uses respirators of 1000 APR or higher in all situations involving potential worker exposures to MC during pharmaceutical production processes and believes that this is widely (and perhaps universally) the case within the industry. • EPAs current assumptions substantially overstate the risks to workers and should be revised to reflect actual practices in the industry. Those practices do, in fact, protect workers against exposure to unreasonable health risks.	process, EPA has determined that this use falls outside TSCA's definition of "chemical substance." 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 found that methylene chloride use as a functional fluid in a closed system during pharmaceutical manufacturing entails use as an extraction solvent in the purification of pharmaceutical products, and has concluded that this use falls within the aforementioned definitional exclusion and is not a "chemical substance" under TSCA (section 5.3).
Clarity in the use of PPE assumptions for risk characterization is needed		
73, 66	**PUBLIC COMMENTS:** • In the "Risk Considerations" section for each entry in Table 5-1, the following statement: "EPA does not expect routine use of respiratory PPE sufficient to mitigate risk" appears for several conditions of use. However, in some cases, later in the same "Risk Considerations" section, EPA states that its risk estimates "do not indicate risk when expected use of PPE was considered". These statements appear contradictory and clarity is needed. • The meaning of parenthetical statements such as "(respirator APF 25)" or "(for central tendency, respirator APF 25)" was not explained and is unclear. • In Table 5-1, a number of the risk estimates are presented with PPE (pp. 430-431, for example). This seems to go against the discussion earlier, which appeared to state that risk estimates would be done without PPE to be more health protective and also contradicts the initial statement that EPA does not expect routine use of respiratory PPE.	In response to these comments, EPA has revised and clarified the language used in the unreasonable risk determinations in section 5. The details of the considerations in the unreasonable risk determinations for each condition of use now more clearly state when EPA assumes use of PPE, what APF or PF is assumed, and how the risk estimates support or do not support a determination of unreasonable risk for that condition of use. EPA also describes the other factors considered when making determinations of unreasonable risk. While Table 5-1 in the final risk evaluation presents different information than in the draft risk evaluation, EPA is consistent in incorporation of 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

	• In some cases, the risk estimates EPA listed for workers (and ONUs) in Table 5-1 fail to include those for cancer, which frequently indicate excessive risk relative to EPA's 10^{-4} cancer risk benchmark when respiratory PPE is not assumed. • It is essential that EPA's risk determinations accurately reflect the risk estimates that EPA derived for each exposure scenario and health endpoint where EPA found excessive risk relative to its benchmarks. Accurate accounting of the risk estimates that EPA used to determine whether it found unreasonable risk and to characterize the nature, magnitude and extent of the risk EPA found is vital for the transparency of EPA's decisions.	has also outlined its PPE assumptions in section 5.1. Further, in the final risk evaluation for MC, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE. Regarding the cancer risk estimates, all risk estimates are now presented in Table 4-2 for workers and 4-3 for consumers, and were considered along with other factors during the determinations of unreasonable risk.
73	**PUBLIC COMMENTS:** • For 8 of its 65 conditions of use, EPA dismissed an unreasonable risk to workers by invoking PPE that the Agency had already stated is not expected to be used. Conversation with EPA staff indicate this contradictory approach appears to have been a mistake, but they are presented here to ensure that they are corrected. All of these cases involved cancer risks. • In each case, EPA's risk estimation tables in Chapter 4 of the draft risk evaluation identified and boldfaced a risk estimate that exceeded EPA's risk benchmark; yet, these risks were not identified in the corresponding section of Table 5-1 in EPA's risk determinations. Instead, EPA appears to have invoked expected use of PPE as the explanation. • In two other cases, EPA dismisses an unreasonable risk with no explanation. • In all 10 of these, EPA's conclusions run contrary to the evidence before the Agency. Based on the analysis presented in the draft risk evaluation, EPA	EPA has reviewed all the risk determinations in the draft risk evaluation to correct any inconsistencies in the approach for determining unreasonable risk, including considering the use of PPE in each condition of use. In response to this comment, EPA has revised the structure of the unreasonable risk determination section and the presentation of the unreasonable risk determination for each condition of use, for greater clarity and to prevent the appearance of any contradictions. EPA's approach for developing exposure assessments for workers is to use the reasonably available information to construct exposure scenarios that are anchored in the real-world use of chemicals. 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

	should find an unreasonable risk to workers or ONUs presented by these conditions of use.	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 MC, EPA has determined that most conditions of use pose an unreasonable risk to workers even with the assumed PPE. EPA's assumption that workers are typically protected by PPE is based on consideration of the OSHA regulations at 29 CFR 1910.1052, which sets the methylene chloride standard, including which circumstances necessitate the use of personal protective equipment (PPE). Thus, 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.
General potentially exposed or susceptible subpopulation considerations		
SACC, 66	**SACC COMMENTS:** • Several Committee members requested additional clarification on the handling of potentially exposed or susceptible subpopulations within the TSCA risk evaluation approach and especially with respect to the setting of UFs. • The risk evaluation should define and assess worker subpopulations that would be expected to have	EPA describes potentially susceptible subpopulations in Section 4.4 (Potentially Exposed or Susceptible Subpopulations), including tobacco smokers. EPA uses PBPK models for toxicokinetic differences (for chronic risk) and intraspecies UFs in the risk evaluation; the intraspecies UF was established to account for uncertainty and variability that includes susceptible subpopulations (EPA, 2002). Research indicates that a factor of 10 (when including both toxicokinetics and toxicodynamics) is sufficient in most

	enhanced inhalation intake, such as tobacco smokers. **PUBLIC COMMENTS:** • Section 4.3 has a good discussion of potentially vulnerable populations, but it's not clear in this section how some of those vulnerabilities (genetic polymorphisms, current smoking, etc.) are factored into the risk assessment. • Fetuses, infants, and toddlers are briefly mentioned, but it's not clear that their risk was modeled at all in the risk assessment.	cases (EPA, 2002), and EPA expects that the UFs and PBPK models used in the risk evaluation are sufficient for the identified subpopulations applicable to methylene chloride.
54	**PUBLIC COMMENTS:** • The draft evaluation underscores the greater vulnerability of certain population groups to the risks of CNS depression, coma, and death from acute exposure to MC. These groups include pregnant women, the elderly, fetuses, children, people engaged in vigorous physical activity, users of alcohol, and individuals suffering from lung and heart disease. EPA argues that it has accounted for the higher susceptibility of these groups by applying a default intraspecies uncertainty/variability factor (UF) of 10. However, this UF is normally used for expected variations in response among a healthy population and may not be protective for subgroups known to be a risk of acute effects at lower levels of exposure than healthy adults.	EPA considers the intraspecies UF of 10 for the CNS endpoint from acute exposure to be sufficient; this UF was established to account for uncertainty and variability that includes susceptible subpopulations (EPA, 2002). Research indicates that a factor of 10 is sufficient in most cases (EPA, 2002), and EPA expects that the UFs and PBPK models used in the risk evaluation are sufficient for the identified subpopulations applicable to methylene chloride.
73, 44, 75, 72, 55, 43	**PUBLIC COMMENTS:** • EPA has not met its mandatory duty under TSCA to thoroughly identify and evaluate the risks to vulnerable subpopulations. • Due to the developmental neurotoxicity risks, pregnant women, fetuses, and children should all be specifically included. EPA could have been more health-protective by considering non-regular exposures to MC for infants and toddlers.	EPA uses PBPK models for toxicokinetic differences (for chronic risk) and intraspecies UFs in the risk evaluation. The intraspecies UF was established to account for uncertainty and variability that includes susceptible subpopulations (EPA, 2002). Research indicates that a factor of 10 (when including both toxicokinetics and toxicodynamics) is sufficient in most cases (EPA, 2002), and EPA expects that the UFs and PBPK models used in the risk evaluation are

	• Due to the reproductive risks, reproductive aged men and women should be included. • Due to the risks for neurotoxicity, immunotoxicity and other risks, elders and people with health conditions should be included. Because of MC's conversion to CO, people engaged in vigorous physical activity, users of alcohol and individuals suffering from lung and heart disease should be included.	sufficient for the identified subpopulations applicable to methylene chloride. At the beginning of section 2.4.1, EPA states that for the purpose of this assessment, EPA considered occupational exposure of the total workforce of exposed users and non-users, which include but are not limited to male and female workers of reproductive age who are >16 years of age. Female workers of reproductive age are >16 to less than 50 years old. Adolescents (>16 to <21 years old) are a small part of this total workforce. The occupational exposure assessment is applicable to and covers the entire workforce who are exposed to MC. There was no upper limit on male reproductive age assumed for this evaluation. For methylene chloride consumer exposure evaluation, inhalation exposures are presented as concentrations encountered by users and bystanders independent of age-group considerations, while dermal exposures are presented for users in three age groups that would be inclusive of reproductive aged men and women (ages 11-15; ages 16-20, and 21+)
Potentially exposed or susceptible subpopulation considerations for the general population		
SACC	**SACC COMMENTS:** • The impact of MC emissions to the ambient air, including population exposures living in close proximity to large and small emission sources of MC. These populations can be considered potentially exposed subpopulations in the context of potentially exposed or susceptible subpopulations.	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 methylene chloride 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.
64, 73, 75, 44	**PUBLIC COMMENTS:** • Long-term exposure to MC through the ambient air pathway is an area of concern for the South Coast Air Quality Management District (AQMD), especially for residents and sensitive receptors located close to facilities using MC or temporary worksites where there is use of MC-containing materials. • ATSDR emphasizes that "groups within the general population that could have potentially high exposures… include individuals living in proximity to sites where MC was produced or sites where methylene chloride was disposed, and individuals living near 1 of the 1,569 NPL hazardous waste sites where methylene chloride has been detected in some environmental media (HazDat 1996)." • In the 2018 MC Problem Formulation document, EPA stated that it expects to consider in the risk evaluation "other groups of individuals within the general population who may experience greater exposures due to their proximity to conditions of use. Such consideration was not presented in the	• EPA did not consider background exposure that workers and consumers using products containing MC might be exposed to in addition to exposures from TSCA-regulated conditions of use. 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 examined

	draft risk evaluation document, and instead, the EPA assumed that its other environmental statutes – such as the CAA – adequately assess and effectively manage these other exposure pathways. • We disagree with this assumption and are concerned that risks to individuals living or working near manufacturing, processing, use or disposal sites could be substantial. • EPA provides no analysis of whether those living in proximity to the conditions of use are at greater risk due to greater exposure. EPA should analyze these exposures and should analyze these potentially exposed subpopulations. • EPA should also identify people living near all disposal sites as potentially exposed or susceptible subpopulations. These groups include (but are not limited to) those living near Superfund sites. Many disposal sites are associated with activities that reflect ongoing or prospective manufacturing, processing, distribution, or use, so EPA must also analyze those disposals and disposal sites and populations living in proximity to them.	how methylene chloride 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.
66	**PUBLIC COMMENTS:** • Chapter 5 (p. 425) notes that high-end risk estimates (i.e., 95th percentile) are generally intended to cover individuals or sub-populations with greater exposure. This may be the best available alternative but may not address smaller subpopulations that have very different risk profiles.	To address potentially exposed subpopulations, the range of use patterns evaluated (10th to 95th percentile) is expected to cover the reasonable range of possible exposures. To address susceptible subpopulations, EPA has relied in PBPK models (for chronic risks) as well as uncertainty factors (for noncancer acute and chronic risks), and the lower 95th percent confidence limits on the dose-response model (for cancer), in accordance with existing guidance (EPA, 2005b, 2002).
Workers are a potentially exposed or susceptible subpopulation		
73, 69, 72	**PUBLIC COMMENTS:** • EPA is required to protect workers, both generally and as a "potentially exposed or susceptible subpopulation," under TSCA, not under OSHA.	• EPA recognizes that the PEL is a technology-based limit, rather than a risk-based limit and that there may be health risks in some cases from exposures below the PEL. • As noted in the draft risk evaluation, EPA relied on

	• There are considerable gaps in the OSHA standard that leave some particularly vulnerable workers unprotected (e.g., small businesses or individual contractors). EPA cannot claim the OSHA standard is sufficient to remove unreasonable risks to workers as it does not improve workplace compliance over time, allows an appreciable cancer risk that is unreasonable as per EPA standards, and does not protect all worker populations. EPA is obligated under TSCA to take action to mitigate unreasonable risks. • The 2016 amendments to TSCA strengthened EPA's already-existing mandate to protect workers. TSCA's new definition of "potentially exposed or susceptible subpopulation" has no asterisk next to workers, and there is no basis in TSCA for EPA to provide less protection to workers than any other such subpopulation, let alone than the general population. Yet that is exactly what EPA has done here. • EPA represents its high-end estimates as "generally intended to cover individuals or sub-populations with greater exposure," while its central tendency estimates apply to the "average or typical exposure" that people experience (p. 425). TSCA would not permit EPA to protect against only the "average or typical exposure;" in fact, when it comes to workers and other "potentially exposed or susceptible subpopulations," EPA is required to protect all of them.	NIOSH guidance when choosing the 10^{-4} cancer risk benchmark to evaluate risks to workers from methylene chloride exposure. • The range of use patterns evaluated (10th to 95th percentile) is expected to cover the reasonable range of possible exposures. • 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 judgement underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. 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. 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 as well as to capture exposures for PESS. EPA has also outlined its PPE assumptions in section 5.1.
Consideration of potentially exposed or susceptible subpopulations and genetic polymorphisms		
SACC	**SACC COMMENTS:** • GST-T1 genotype plays an important role in individual response to MC exposures. This defines (genetically and proportionately) a specifically	EPA added more information to the risk evaluation to explain that this population is expected to be protected based on use of the 95% lower confidence limit on the cancer slope factor.

	susceptible subpopulation that should be further discussed in the risk evaluation.	
44, 49, 72, 75	**PUBLIC COMMENTS:** • In particular people with the GST-T1 +/+ genotype – who comprise approximately 1/3 of the U.S. population, and thus also represent a significant proportion of the workforce – "are expected to be more susceptible to cancer endpoints. EPA failed to protect these sensitive subpopulations in its risk characterization."	EPA added more information to the risk evaluation to explain that this population is expected to be protected based on use of the 95% lower confidence limit on the cancer slope factor.
Consideration of potentially exposed or susceptible subpopulations and cardiovascular disease		
69, 49, 44, 75, 72	**PUBLIC COMMENTS** • EPA's quantitative calculations of risk do not account for the increased susceptibility of those with cardiovascular disease to MC acute toxicity, including higher risk of myocardial infarction and fatality. In addition, MC's metabolite, CO, has well-documented ischemic and arrhythmogenic cardiac effects. MC can also directly sensitize the myocardium to arrhythmias. • This risk group constitutes a large proportion of the population and EPA should add a data-derived or default adjustment factor to its risk calculations.	EPA considers the intraspecies UF of 10 for the CNS endpoint from acute exposure to be sufficient; this UF was established to account for uncertainty and variability that includes susceptible subpopulations (EPA, 2002). Research indicates that a factor of 10 is sufficient in most cases (EPA, 2002), and EPA expects that the UFs used in the risk evaluation are sufficient for the identified subpopulations applicable to methylene chloride. Sensitization of the myocardium to ventricular tachycardia occurs at concentrations of 25,000 ppm, and therefore the POD of 195 ppm is expected to protect against this effect.
Potentially exposed or susceptible subpopulations and developmental toxicity/neurotoxicity		
55, 73, 44, 75, 57	**PUBLIC COMMENTS:** • EPA does not evaluate risks to fetuses and infants or calculate its PODs with them in mind. • Neurotoxic and cardiovascular effects may be exacerbated in fetuses and infants with higher residual levels of fetal hemoglobin when exposed to high concentrations of methylene chloride; however, developmental neurotoxicity risks are not addressed. • With regard to the acute MOE, the Bornschein et al. (1980) neurodevelopmental study revealed effects	EPA uses PBPK models for toxicokinetic differences (for chronic risk) and intraspecies UFs in the risk evaluation. The intraspecies UF was established to account for uncertainty and variability that includes susceptible subpopulations (EPA, 2002). Research indicates that a factor of 10 (when including both toxicokinetics and toxicodynamics) is sufficient in most cases (EPA, 2002), and EPA expects that the UFs used in the risk evaluation are sufficient for the identified subpopulations applicable to methylene chloride.

	but did not identify a NOAEL. This calls into question whether the hazard values (PODs) for acute exposure occupational and consumer scenarios are adequately protective for the fetus (in the case of exposures to pregnant women) as well as infants and children. • EPA did not apply any additional UFs to address sensitive developmental neurotoxicity endpoints, which can be much more sensitive than systemic impacts like fecundity and fetal resorption. • Conclusion: Based on these findings, we assert that the current system in the United States for evaluating scientific evidence and making health-based decisions about environmental chemicals is fundamentally broken. To help reduce the unacceptably high prevalence of neurodevelopmental disorders in our children, we must eliminate or significantly reduce exposures to chemicals that contribute to these conditions. We must adopt a new framework for assessing chemicals that have the potential to disrupt brain development and prevent the use of those that may pose a risk. This consensus statement lays the foundation for developing recommendations to monitor, assess, and reduce exposures to neurotoxic chemicals. These measures are urgently needed if we are to protect healthy brain development so that current and future generations can reach their fullest potential.	TSCA requires EPA to use reasonably available information and best available science in its risk evaluation. Utilizing the systematic review process, EPA used reasonably available data and best science in a weight of scientific evidence analysis.
75	**PUBLIC COMMENTS:** • The draft MC evaluation does not mention placental transfer as an additional risk factor for fetuses. Because fetuses are already more vulnerable to the neurotoxic effects of elevated CO than healthy adults, even where fetal exposures may be lower	EPA uses PBPK models for toxicokinetic differences (for chronic risk) and intraspecies UFs to account for variation in sensitivity within the human population. The intraspecies UF was established to account for uncertainty and variability that includes susceptible subpopulations (EPA, 2002). Research indicates that a factor of 10 (when including both toxicokinetics and toxicodynamics) is sufficient in most

	than maternal exposures, the effects on the fetus are likely to be much more severe and even deadly. • Use of an additional UF to address to address greater susceptibility to MC's CNS effects during early-life exposure is consistent with the similarly enhanced UFs recommended in EPA's Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens.	cases (EPA, 2002), and EPA expects that the UFs used in the risk evaluation are sufficient for the identified subpopulations applicable to methylene chloride, including fetuses.
Cancer risk benchmark		
49, 73, 42, 70, 75, 69, 72	**PUBLIC COMMENTS:** • EPA cites NIOSH guidance and the Benzene decision for support of the cancer risk benchmark (p. 426, footnote 23), but that guidance and that case pertain to how the standard for health protection is applied under OSHA, not under TSCA. • The 2016 amendments to TSCA also explicitly preclude EPA from considering feasibility or other non-risk factors when determining whether a chemical presents an "unreasonable risk," including to workers; see TSCA Section 6(b)(4)(A). Yet EPA invokes standards under other statutes that lack this prohibition in an effort to claim precedent for its 1 x 10^{-4} benchmark (p. 426, footnote 22). • EPA invokes the "two-step approach" used under the CAA, where EPA includes a "limit on maximum individual lifetime [cancer] risk (MIR) of approximately 1 in 10 thousand" (p. 426 n. 22, citing 54 Fed. Reg. 38,045 (September 14, 1989)) and consideration of whether emissions standards provide an ample margin of safety to protect public health "in consideration of all health information, including the number of persons at risk levels higher than approximately 1 in 1 million, as well as other relevant factors."	As noted in the draft risk evaluation (Section 5.1.1), EPA relied on NIOSH guidance (Whittaker et al., 2016) when choosing the 10^{-4} cancer risk benchmark to evaluate risks to workers from methylene chloride exposure. NIOSH's mandate, on pg iii of Whittaker et al. (2016), is to: "… describe exposure levels that are safe for various periods of employment, including but not limited to exposure levels at which no employee will suffer impaired health or functional capacities or diminished life expectancy as a result of his work experience." Although NIOSH guidance, p. 20, states that: "exposures should be kept *below* a risk level of 1 in 10,000, *if practical* [emphasis added]" EPA adheres to the 1 in 10,000 benchmark during the risk evaluation stage for TSCA chemicals. Note that other precedents (e.g., Office of Water; Office of Air) are the basis for cancer benchmarks to be used for risks to the general population, but EPA did not evaluate such scenarios for MC. EPA has considered susceptible subpopulations when evaluating these risks, as directed by TSCA. Specifically, EPA used the lower 95th confidence bound on the cancer slope, which accounts for variability and uncertainty in individuals' tumor responses, including susceptible subpopulations.

	• EPA likewise uses a risk range of 1 x 10^{-4} to 1 x 10^{-6} to set cleanup goals at CERCLA hazardous waste sites. EPA's recent draft risk evaluations deviate from this approach for worker exposures, maintaining that risks smaller than 1 x 10^{-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" (p. 426). • EPA fails to explain why OSHA precedent should control decision-making under TSCA. In contrast to OSHA, TSCA provides protections to workers not just from chemical exposure in the workplace, but also from air emissions and other environmental releases as well as exposures to consumer products. • In this risk evaluation, EPA has set a risk level for the entire worker population that is the same as the level EPA elsewhere set for the most exposed individual in a population. EPA then erroneously invokes this level repeatedly to find a number of conditions of use of MC to pose no risk to any workers, thereby subjecting many tens of thousands of workers to cancer risks that are as much as two orders of magnitude higher than warranted. This approach must be rejected on scientific as well as legal grounds. • The cancer risk benchmark level EPA uses for workers that fails to protect them as a vulnerable subpopulation as required by TSCA. EPA must apply to workers the same benchmarks for determining unreasonable cancer risks that it uses for other populations. For all exposed populations, the goal should be to protect against cancer risks exceeding 1 x 10^{-6}.	Consistent with 2017 NIOSH guidance, EPA used $1x10^{-4}$ as the benchmark for the purposes of this unreasonable risk determination for individuals in industrial and commercial work environments. It is important to note that $1x10^{-4}$ is not a bright line and EPA has discretion to make unreasonable risk determinations based on other benchmarks or factors as appropriate. See section 5.1.1.2 of the risk evaluation for additional information. For the purposes of unreasonable risk determinations, EPA is assuming the use of PPE on a case-by-case basis for each COU and the context of how it is used (i.e., industrial, commercial, consumer), in contrast to the approach EPA would take in a regulatory action, which would protect against workplace hazards by requiring certain actions to address the unreasonable risk. EPA also distinguished between the methods for risk evaluation and the "protection" measures that are the goal of risk management actions.

73, 75	**PUBLIC COMMENTS:** • EPA's occupational risk estimates were dramatically impacted by EPA's selection of 10^{-4} as the cancer risk benchmark. • To determine how large the impact is, EPA's cancer risk estimates for each of its 65 conditions of use involving inhalation exposures to workers and ONUs and each of its 23 OESs involving potential dermal exposures to workers were examined. Collectively, this analysis shows that EPA's draft risk evaluation has dramatically understated the occupational cancer risks of MC (specific examples were given).	As noted in the draft risk evaluation, EPA relies on NIOSH guidance when choosing the 10^{-4} cancer risk benchmark to evaluate risks to workers from methylene chloride exposure. EPA, consistent with 2017 NIOSH guidance, used $1x10^{-4}$ as the benchmark for the purposes of this risk determination for individuals in industrial and commercial work environments. 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. It is important to note that $1x10^{-4}$ is not a bright line and EPA has discretion to make unreasonable risk determinations based on other benchmarks or factors as appropriate. See section 5.1.1.2 of the risk evaluation for additional information.
Risk to ONUs		
SACC, 49, 73, 72, 75	**SACC COMMENTS:** • In its review of the resulting risk estimate for chronic exposure of ONU for two scenarios (repackaging and plastic and rubber product manufacturing), the risk evaluation reports: "... In consideration of the uncertainties in the exposures for ONUs for this condition of use, EPA has determined the non-cancer risks presented by chronic inhalation are not unreasonable" (pp. 432 and 436). • The justification for this statement is the use of the pre-1997 updated OSHA PEL exposure data. This justification seems arbitrary, given that pre-1997 data was used to estimate exposure for fabric finishing and spot cleaning. Since the risk evaluation establishes the need and utility of the pre-1997 data in one case, it should also use all the data for repackaging and plastic and rubber product	In section 4.3.2.1, EPA states the uncertainty of the use of data from before the PEL revision and that use of some older data may overestimate some exposures. EPA revised text in 2.4.1.1 to expand upon adequacy of older data and summarize EPA's new statistical analysis, which is included as a new appendix in the Supplemental Information on Releases and Occupational Exposure Assessment. This supplemental document also presents all data found for each use and provides rational for whether data were acceptable or not. EPA considers occupational non-users (ONUs) to be a subset of workers for whom the potential inhalation exposures may differ based on proximity to the exposure source. For the majority of MC conditions of use, the difference between ONU exposures and workers directly handling the chemical cannot be quantified. EPA assumed that, in most cases, ONU

	manufacturing. Alternatively, the risk evaluation should explicitly state under what conditions data do not represent exposure (or hold too much uncertainty) prior to the risk determination stage. • Recommendation: Be more explicit and consistent with respect to what data are deemed usable for the determination of exposure and risk. **PUBLIC COMMENTS:** • EPA fails to properly account for risks to so-called ONUs, because the range of workers defined by EPA as ONUs (supervisors, managers, engineers, and other personnel in nearby production areas) is too broad to warrant a single categorization • EPA applied the flawed approach that even if it found excessive risks in some cases for high-end exposures, it could still determine that the risk was not unreasonable as long as the risks of the corresponding central tendency exposures did not exceed its benchmarks. • This assumption alone, which has no support in the record, resulted in multiple determinations of no unreasonable risk for ONUs. If EPA treated ONUs similarly to other workers, the risks presented by this condition of use would be nearly 20 times lower than the benchmark MOE. • This is not theoretical: EPA has ignored exceedances of its risk benchmarks for acute, chronic and/or cancer effects by high-end exposures to ONUs for at least 19 of its 65 conditions of use; for examples, see pp. 431, 436, 449.	inhalation exposures are assumed to be lower than inhalation exposures for workers directly handling the chemical substance. In several instances, monitoring data or modeling did not distinguish between worker and ONU inhalation exposure estimates. To account for this uncertainty, EPA considered the workers' central tendency risk estimates from inhalation exposures when determining ONU unreasonable risk. For dermal exposures, EPA assumed that ONUs do not have direct contact with methylene chloride; therefore, non-cancer effects and cancer from dermal exposures from methylene chloride generally were not identified. For inhalation exposures, EPA, where possible, estimated ONU exposures and described the risks separately from workers directly exposed.
66	**PUBLIC COMMENTS:** • In chapter 5, line 9910 on p. 431, the article stated that it poses an unreasonable risk to occupational non-users that would be exposed to it. Protective measures should be in place or lowering of the standard would be in order, rather than risk people	During the risk management process, which follows the risk evaluation, EPA identifies and proposes risk management options for the unreasonable risks EPA has determined are presented.

	in an occupational health setting to this exposure without their knowledge.	
Exclusions in the MC draft risk evaluation		
75	**PUBLIC COMMENTS:** • EPA's position that other environmental laws should displace TSCA risk evaluations arbitrarily assumes that these laws provide equivalent protection of public health and the environment and that there is no added benefit in evaluating the risks presented by environmental pathways of exposure under TSCA. • TSCA's strict risk-based framework for chemical risk management is not mirrored in most environmental laws that govern releases to air, water, and soil and disposal of waste.	Clarifying language about what pathways are addressed under other statutes has been added to Section 1.4.2 of the Risk Evaluation.
49, 73, 64	**PUBLIC COMMENTS:** • In the problem formulation for MC (pp. 43-44), EPA explicitly relies on the CAA to dismiss the need to assess exposures to MC from air emissions. MC is regulated as a HAP under the CAA, but the standards under the CAA for HAPs are set for individual source categories, meaning that the exposures to MC from all sources in combination are never considered. • Unlike considerations under TSCA, EPA is required to consider cost in establishing standards for HAPs, resulting in a less stringent risk analysis under CAA authority than that under TSCA review. • It is recommended that the EPA establish clear enforcement mechanisms for its standards and allow state and local regulatory agencies the authority to enforce them.	Clarifying language about what pathways are addressed under other statutes has been added to Section 1.4.2 of the Risk Evaluation.
66, 76, 33, 49, 73, 77	**PUBLIC COMMENTS:** • EPA's ongoing failure to consider all contexts in which exposure to MC create the risk of cancer, injury to the reproductive system, or other harms to	Clarifying language about what pathways are addressed under other statutes has been added to Section 1.4.2 of the Risk Evaluation.

	human health and the environment puts our residents at risk, contradicts TSCA's requirements, and fails to satisfy reasonableness standards. • EPA is thus required to evaluate all of the risks associated with a chemical's known, intended, and reasonably foreseen conditions of use, regardless of whether such risks are or may be regulated under another statute. Even if other statutes can address some of these risks to some extent, EPA cannot evaluate, as it purports to do here, the total, cumulative risk to public health and the environment from these chemicals if it excludes exposures through these other pathways To do so would render any evaluation partial and incomplete. • This assault on TSCA is illegal, and goes against the science that informs what we know about how chemicals like MC can affect our health and the environment. EPA's delegated authority under TSCA does not allow it to focus only on "the greatest areas of concern to EPA." EPA must evaluate all exposure pathways, including those regulated by other statutes.	
SACC, 49, 55, 72, 73, 75	**SACC COMMENTS:** • The Committee discussed the need for data on neurotoxicity on outcomes such as CNS depression and cognitive deficits. **PUBLIC COMMENTS:** • EPA's decision not to develop risk estimates for reproductive/development effects, developmental neurotoxicity, immunotoxicity, and endocrine effects is effectively a recognition that it cannot make unreasonable risk determinations under TSCA Section 6(b) for these endpoints using currently available data.	EPA had sufficient information to complete the MC risk evaluation using a weight of scientific evidence approach. Data are available for the endpoints identified were not recommended for use in the dose-response analysis. 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

	• EPA's obligation under TSCA is to address all conditions of use, hazards and routes of exposure in its risk evaluations. • EPA did not use its information-gathering authority when preparing the draft MC risk evaluation, even in circumstances where EPA itself described the existing data as inadequate and despite identifying the absence of data for critical endpoints in its 2011 IRIS assessment and 2014 Work Plan risk assessment. • Any risk evaluation that EPA now finalizes without sufficient data for all endpoints would be incomplete and inadequate. EPA must act expeditiously to require the necessary testing under Section 4 and make an unreasonable risk evaluation for the health effects it is now unable to address.	assessed under TSCA. EPA addresses all conditions of use for MC.
Environmental risk characterization		
SACC, 73, 49, 75, 66	**SACC COMMENTS:** • Five out of 21 (23.8%) manufacturing facilities examined in the assessment were found to pose risk to aquatic organisms. Given that in 2019 there were 81,654 facilities reporting disposal of MC, it is quite possible that many these facilities, if examined, would also be found to pose an unreasonable risk. • This admittedly simplistic extrapolation suggest that MC releases pose an unreasonable risk for environmental/aquatic receptors simply because of the large numbers and geographical spread of manufacturing facility releases. • EPA should acknowledge the implications of this extrapolation in its environmental risk characterization. **PUBLIC COMMENTS:** • EPA cannot reasonably dismiss its findings of environmental risk merely by invoking uncertainty.	• EPA considered facilities that release methylene chloride and did not find unreasonable risk to the environment for any condition of use based on risks to aquatic, sediment-dwelling, and terrestrial organisms. • It should be noted that it is unclear where the SACC member identified 81,654 facilities reporting disposal of MC. The number is not in the methylene chloride risk evaluation. • EPA modeled the TRI data and considered the waste treatment of the facilities, the ambient water concentrations, the biological relevance of the species (e.g. for one facility it releases to an estuarian environment, and the acute RQ is based on amphibian data. Because amphibians reside in freshwater environments, acute risk to amphibians is unlikely at this facility), and frequency and duration of the exposure (e.g., in many instances the releases were indirect) to determine if the RQs indicated risk.

	For environmental risk, EPA's own analyses showed that MC presents an unreasonable risk to aquatic organisms (pp. 389, 286-87), but EPA dismisses this unreasonable risk by invoking uncertainty without further explanation (pp. 32, 428). • This approach is arbitrary and capricious because EPA refuses to accept the outcomes of its own analyses, and EPA's conclusions run contrary to the evidence before the agency. Based on the analysis presented in the draft risk evaluation, EPA should find an unreasonable risk to the environment presented by certain disposal and recycling conditions of use. • EPA also discounts the results of its own calculations that indicate unreasonable environmental risks. Despite its exclusions of data and averaging of results, EPA still calculated multiple RQs >1, the general threshold for unreasonable risk (p. 425). • In its draft risk evaluation, EPA concludes that MC does not pose an unreasonable risk to the environment. However, it reaches this conclusion by excluding the studies that demonstrate the greatest environmental risk, obscuring the results of the studies that it does consider, and disregarding RQs more than 100 times greater than EPA's unreasonable risk threshold. • EPA also dismisses the evidence of harmful contamination with the following: "No acute or chronic risks to aquatic organisms were identified in ambient water; therefore, the risks identified for the five facilities mentioned above are likely localized to surface water near the facility" (p. 389). EPA provides no information on how large an area it considers to be 'ambient' or 'localized' or – most	• At the suggestion of the SACC, because the E-FAST model does not consider chemical fate or hydrologic transport properties and may not consider dilution in static water bodies, EPA conducted an analysis of fugacity modeling and a more robust discussion of these uncertainties was added to the risk evaluation. Given the uncertainties about waterbody depth, flow, temperature, etc. there is some uncertainty about how long the half-life of MC will be in various water bodies (section 4.4.6). The analysis indicated that model outputs may best represent concentrations found at the point of discharge, and there is lower confidence in concentration estimates the farther they are from the facility. Additionally, EPA added more discussion of how large an area is considered "ambient" and "localized." Discussion of other uncertainties was also included, such as limitations in data, since monitoring data were not available near facilities where methylene chloride is released, TRI does not capture release data for facilities with fewer than 10 employees, and only one year of release data was evaluated. • While some site-specific RQs, calculated from modeled release data from particular facilities conducting recycling, disposal, and waste water treatment plant activities, are greater than or equal to 1, indicating risk, uncertainties related to these particular estimates (discussed broadly above and specifically in section 4.2.2) support a determination of unreasonable risk for the environment.

	importantly – why risks to aquatic species in contaminated waters near facilities can be disregarded in determining unreasonable risks to the environment under TSCA.	
Is the draft risk evaluation protective?		
SACC, 49, 73, 66, 75	**SACC COMMENTS:** • One Committee member suggested that very likely the Evaluation underestimates risk during the process of risk characterization. • The target MOEs were not sufficiently large to capture the uncertainties in the assessment (such as e.g., GST polymorphisms, database UFs) and thus conclusions of no unreasonable risk, for example for ONUs, cannot be adequately supported. • In the spirit of protecting public health, the Committee member invited the Agency to acknowledge the unaccounted sources of uncertainty and as a result include more scenarios in the unreasonable risk category. • In several parts of the risk evaluation, the possibility of both overestimation and underestimation are discussed. One Committee member cautions that overestimation in one part of the risk characterization calculation and underestimation in another part do not cancel each other out. The two errors are not the same and do not carry the same weight in terms of human health risk assessment. **PUBLIC COMMENTS:** • In its draft risk evaluations, EPA has not only understated MC risks, but also mischaracterized the risks that it has calculated. EPA repeatedly finds that risks that fall below the benchmark MOE or that exceed EPA's cancer threshold are nonetheless reasonable and need not be managed under TSCA. • In this risk evaluation EPA has re-instituted a flawed approach, under which it can still deem a	EPA uses PBPK models for toxicokinetic differences (for chronic risk) and intraspecies UFs (for non-cancer risks) in the risk evaluation. The intraspecies UF was established to account for uncertainty and variability that includes susceptible subpopulations (EPA, 2002). Research indicates that a factor of 10 (when including both toxicokinetics and toxicodynamics) is sufficient in most cases (EPA, 2002), and EPA expects that the UFs used in the risk evaluation are sufficient for the identified subpopulations applicable to methylene chloride. 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. Such consideration carries extra importance when the risk estimates are close to the benchmarks for risks from acute and chronic non-cancer health effects and cancer.

	risk to be reasonable even though it exceeds the applicable acceptable level, as long as it is "close" to the acceptable level. • EPA applies this in only one direction in the draft risk evaluation. Even where EPA's estimated MOEs are only slightly greater than the benchmark MOE, EPA still finds no unreasonable risk.	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, which include assumptions regarding PPE use, 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 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. EPA uses the high-end exposure value when making its unreasonable risk determination in order to address uncertainties around PPE usage as well as to capture exposures for PESS. Because EPA is making its unreasonable risk determinations on the high-end exposure value for workers and consumers and either the high-end exposure value or central tendency for ONUs, depending on the data, and factoring in the uncertainties due to UF factors, it is unclear how this is a flawed approach. Additionally, EPA makes an unreasonable risk determination and makes no determination on reasonable risk.
69	**PUBLIC COMMENTS:** • Our research on MC fatalities finds current policies inadequate to protect workers and recommends elimination of MC use in commercial settings.	Thank you for your comment.
73	**PUBLIC COMMENTS:** • Of particular concern is that EPA's current draft risk evaluation is less health-protective than its 2014 MC Work Plan risk assessment. EPA's risk estimates backslides by a factor of 2 (relying on a benchmark MOE = 30 as opposed to 60). • EPA also uses the far less health-protective cancer risk benchmark of 10^{-4} instead of 10^{-6} (see Section 9.A.ii).	In previous assessments (e.g., the new chemicals program), EPA has applied uncertainty factors of 3 instead of 10 when effects are less severe. Furthermore, IRIS assessments have used default uncertainty factors of 3. In the current risk evaluation, EPA adjusted the LOAEL to NOAEL uncertainty factor to 3 (from a default of 10) to account for the lower severity of effect. As noted in the draft risk evaluation, EPA relied on NIOSH guidance when choosing the 10^{-4} cancer risk benchmark to

		evaluate risks to workers from methylene chloride exposure.
66	**PUBLIC COMMENTS:** • In datasets where there was insufficient data to generate a mean or 95th percentile, EPA made up their own. This could either be too protective or not protective enough. • In Section 4.3.2.1, the potential for overestimation by using the few available air concentration datasets was discussed, and it was difficult to determine whether or not those high values represented actual occupational exposures. This section does not appear to have substantial enough data to be health protective.	EPA had sufficient information to complete the MC risk evaluation using a weight of 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.
66, 73	**PUBLIC COMMENTS:** • If the EPA is attempting to be health protective for the vulnerable populations that would be exposed at higher levels than the general population on a more regular occurrence, these assumptions should be laid out more transparently. • Workers at any facility – whether small, medium, or large – where use of effective PPE cannot be thoroughly documented should be considered vulnerable subpopulations and the risk they face be specifically assessed. For these subpopulations, EPA must determine risk based on exposures without assuming any use of PPE.	The range of use patterns evaluated (10^{th} to 95^{th} percentile) covers the reasonable range of possible exposures.
Risk characterization – general		
73	**PUBLIC COMMENTS:** • EPA failed to analyze distribution in commerce and made unsupported risk findings about this condition of use without a supporting analysis. • EPA's finding on this condition of use has no factual support. It is not supported by substantial evidence or the best available science, and EPA's	For the purposes of the final unreasonable risk determination, distribution in commerce of methylene chloride is the transportation associated with the moving of methylene chloride in commerce. Unloading and loading activities are associated with other conditions of use. EPA assumes transportation of methylene chloride is in compliance with existing regulations for the transportation

	analysis is arbitrary and capricious because it fails to consider this important part of the problem – one of the conditions of use specifically identified by Congress.	of hazardous materials, and emissions are therefore minimal (with the exception of spills and leaks, which are outside the scope of the risk evaluation). Based on the limited emissions from the transportation of chemicals, EPA determines that there is no unreasonable risk of injury to health (workers and ONUs) from the distribution in commerce of methylene chloride.
44, 75	**PUBLIC COMMENTS:** • The draft evaluation addresses 15 consumer products that contain MC. It concludes that these products present acute risks similar in nature and magnitude to the paint remover risks on which EPA based its consumer use ban. • The risk evaluation incorporates verbatim large portions of EPA's 2014 risk assessment and thus reaffirms the rationale for the proposed ban on commercial use of these products that EPA failed to finalize earlier this year.	Thank you for your comment.
69, 77, 71	**PUBLIC COMMENTS:** • EPA has concluded that the vast majority of the conditions of use of MC present an unreasonable risk. But EPA needs to make a determination, under Section 6(b), as to whether MC itself 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 outlined in the implementing regulations for TSCA risk evaluations is consistent with the 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 conditions of use."
71	**PUBLIC COMMENTS:** • EPA's risk evaluation must address commercial use and occupational conditions of use and exposures. • Well-documented occupational risks from commercial uses are not adequately being addressed by EPA as required by TSCA. In March 2019, the Agency also proposed to reassess the feasibility of a training, certification, and limited access program for commercial uses of MC paint and coating	EPA evaluated all conditions of use of methylene chloride under TSCA, including commercial and industrial uses that result in occupational exposures. Risk management activities are outside the scope of the risk evaluation. As the commenter indicated, as appropriate for any condition of use determined to have unreasonable risk, EPA will consider feasibility and implementation of any risk management actions that are proposed to address the unreasonable risks that EPA has determined are presented.

	removal, options that were already analyzed and rejected by the Agency due to inability of these techniques to mitigate unreasonable risks.	In that context, EPA intends to analyze the applicability of any training, certification, and limited access programs.
45	**PUBLIC COMMENTS:** • The use of TWA extrapolation from toxicology studies to schedules for the occupational scenarios is specific to TSCA risk evaluations. The duration averaging approaches for each risk assessment scenario definition should be closely evaluated considering chemical-specific MOA and toxicokinetic data.	As noted in a previous response, EPA understands the uncertainties in using any model but EPA chose the use of the ten Berge equation because even though the lethality data they are based on are not ideal, they do represent an empirically-derived value from inhalation data for solvents. Also, there are several assumptions and uncertainties in the PBPK model described by Bos et al. (2006) that don't warrant using it *instead of* the ten Berge equation: 1) The model accounts for P-450 saturation but P450 saturation occurs at approximately 500 ppm, a value higher than the POD for the current evaluation; 2) The model includes the distribution of GSTT1 in the population but a human study was already used; 3) the parent compound MC has been shown to result in CNS effects in excess of CO/COHb concentrations and Bos et al. (2006) acknowledge that there are no adequate data on MC in rat or human brains; and 4) Bos et al. (2006) state that the model overpredicts MC and COHb concentration by up to 50%.
66	**PUBLIC COMMENTS:** • On several occasions, sources used had likely conflicts of interest from industry making chemical or lobbying group. Other assumptions were made based off one source and from studies made greater than 30 years ago. It would be more prudent to put out a request for more information, especially amongst industrial hygiene groups to assess occupational health exposure limits that monitor hazardous chemicals.	EPA had sufficient information to complete the MC risk evaluation using a weight of 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.

49, 73	**PUBLIC COMMENTS:** • TSCA requires EPA to make a determination as to whether MC, as a whole, presents an unreasonable risk of injury to health or the environment. The extent and magnitude of the flaws in this draft risk evaluation, and the resulting underestimation of risk, mean that EPA has clearly not provided support for any assertion that MC, across all of its conditions of use, does not present unreasonable risk. • Indeed, EPA's determinations that many conditions of use of the chemical do present unreasonable risk can only support a conclusion that the chemical presents unreasonable risk. Moreover, the flaws we have identified make clear that EPA has significantly understated the extent and magnitude of the chemical's unreasonable risk, both overall and for specific conditions of use.	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 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."
66	**PUBLIC COMMENTS:** • The risk assessment only looks at a subset of exposures (acute CNS effects for acute exposure), liver effects, and cancer risks for chronic exposure – although it recognizes that there may be many other health-related effects of MC. The decision was made to focus on these effects due to data limitations, but at least a qualitative discussion of other risks would have provided a fuller picture.	EPA added more information on these uncertainties to Section 4.3.5. - Assumptions and Key Uncertainties in the Human Health Hazards. The risk evaluation also discusses the weight of scientific evidence related to these other effects, including why they were not carried forward to dose-response modeling.

MC	RESPONSE TO COMMENT	
66	**PUBLIC COMMENTS:** • p. 394: The assessment notes that some cancer risks were "very nearly at the benchmarks" for MOE, which both makes the selection of MOE (discussed above) very important, and the characterization of uncertainty very important. These close cases were generally presented as not posting an unreasonable risk, which is not the most health-protective approach. • Chapter 4 Section 2 (related to occupational health exposure): The way it is presented, the set points for the risk estimated were stated but the logic as to how they were calculated was not explained.	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. Such consideration carries extra importance when the risk estimates are close to the benchmarks for acute, chronic non-cancer risks, and cancer risks. The uncertainty factors are described in Section 3.2.5.2 and Tables 4-3 through 4-5 identify that the uncertainty factors are used to set the benchmark MOEs. Page 304 also describes how the uncertainty factors are used to set the benchmark MOE.
68	**PUBLIC COMMENTS:** • EPA should also be more transparent about its consultation and coordination with OSHA when the Agency addresses worker exposures in the risk evaluations, as well as the degree of coordination EPA OPPT had with the Office of Water as required by TSCA Section 9. • A longer term re-thinking of EPA OPPT's approach to coordinating with other EPA program offices, and the establishment of a better process, is in order – both to ensure protection of our air, water and soil and to enable EPA OPPT to meet its statutory obligations to conduct TSCA risk evaluations of high priority chemicals efficiently and in accordance with the best available science.	Thank you for your comment. EPA engages with its federal partners such as OSHA as well as with other offices across EPA to ensure its risk evaluations are well informed and coordinated. EPA will consider this comment for future Risk Evaluations. EPA's discussions and consultation with OSHA are described in section 1.4.4.4 of Supplemental Information on Releases and Occupational Exposure Assessment. Additionally, EPA conferred with OSHA during interagency review and their comments are reflected in the Draft and Final Risk Evaluation
67	**PUBLIC COMMENTS:** • EPA notes in numerous scenarios that their methods likely "overestimate the exposure" based on the data used. However, how this overestimation was considered in the final risk evaluation decision within the MOE calculation is not clear.	EPA considered the key assumptions and uncertainties when determining the overall confidence for the risk estimates.

66	**PUBLIC COMMENTS:** • Sections 4.2 and 4.3 contain some vague statements that make it hard to assess the appropriateness of the decisions (e.g., p. 303: "Different adverse endpoints were determined to be appropriate based on the expected exposure durations;" p. 380: "EPA did not carry immune system effects forward for dose-response because epidemiological, animal and mechanistic data are limited and inconclusive for several reasons.")	Within sections 4.2 and 4.3, EPA added references to other sections (Section 3.2.3, Hazard Identification and Section 3.2.4, Weight of the Scientific Evidence) that contain more detail regarding these decisions.
66	**PUBLIC COMMENTS:** • The tables in Sections 4.6 and 5 – as with those in previous parts of Chapter 4 – are not very transparent. The risk estimates are presented, but it is impossible to follow the calculations without more information.	EPA has added information explaining the data behind several of the risk tables in section 4 and a table explaining PPE assumptions in section 4. Additionally, EPA has reformatted section 5 to increase clarity and transparency.
Suggestions for improving clarity and readability		
SACC	**SACC COMMENTS:** • To aid readability, present findings (e.g., "Risk Conclusion" in Section 4.6) at the beginning of the Risk Characterization section rather than at the end.	EPA has made this change in the MC risk evaluation.
SACC	**SACC COMMENTS:** • Clarification of the statement in p. 383 is requested: "... Because of this the results of risk characterization were generally not sensitive to the individual estimates of the central tendency and high-end separately but rather were based on considering both central tendency and high-end exposure which increase the overall confidence in the risk characterization." • This statement suggests that considering the risks from central tendency and the high-end exposures separately somehow increases confidence in results. • Recommendation: Be more transparent with respect to the decision of using estimates of central	In Section 4.3.2 EPA added a statement saying that where the central tendency and high-end exposure scenarios both had risk, EPA had higher confidence in the risk characterization.

	tendency and high-end jointly as a way to increase confidence in the risk characterization.	
SACC	**SACC COMMENTS:** • Refrain from using the expression "no risk" and use instead the expression "no unacceptable risk" in recognition of the inherent variability and estimator uncertainty associated with assessing even low-risk scenarios. We can never be certain that the true risk is zero.	Unreasonable risk is only used in the unreasonable risk determination section, because it is a legal term under TSCA. Everywhere else EPA states that it identified risk, or it did not identify risk.
Other comments		
62	**PUBLIC COMMENTS:** • There is support for EPA's finding of unreasonable risk of MC in the oil and gas extraction sector and we urge EPA to further investigate and require reporting of emissions from this sector as well.	EPA evaluated the industrial and commercial use of methylene chloride for oil and gas drilling, extraction, and support activities. EPA determined that this condition of use presents an unreasonable risk of injury to health (Section 5.2.1.37). During risk management, EPA will consider which regulatory approaches would address this unreasonable risk, which may include requirements for reporting and recordkeeping.
45	**PUBLIC COMMENTS:** • Flexible foam operation (discussed on p. 144) provides a good example of the issues that arise with grouping non-similar tasks together. This is an example of a failure to use best available science, and it might misinform the risk characterization for "industry application."	EPA did not find reasonably available data to completely prevent grouping of non-similar tasks in many OESs including this OES.
65	**PUBLIC COMMENTS:** • The draft risk evaluation's overstatement of the risks of MC is already discouraging beneficial reclamation of spent MC and encouraging its incineration, contrary to the goals of RCRA. EPA should revise the risk evaluation to more accurately characterize MC's foreseeable TSCA conditions of use and the risks associated with them.	EPA does not agree that there is a need to revise the MC EPA has evaluated all known, intended, or reasonably foreseen conditions of use of methylene chloride and determined whether they present unreasonable risks of injury to health or the environment. EPA's evaluation of these conditions of use, including the reasonably foreseen uses and the recycling that the commenter describes, are based on reasonably available information and best available science. While EPA does not consider non-risk factors for the unreasonable risk determinations in this risk evaluation, the impacts of any risk management actions will

		be considered during any rulemaking to address those unreasonable risks.
62	**PUBLIC COMMENTS:** • EPA has authority to further restrict MC and other VSLS where a substance is listed as Acceptable for end-uses covered by the Significant New Alternatives Policy (SNAP) Program including for solvents, and coatings (see Appendix I). However, this Title VI authority is limited and does not cover risks from the full lifecycle of substances, intermediate uses such as feedstocks, or other end-uses in which Class I and Class II substances were not historically used.	Thank you for your comment.
68	**PUBLIC COMMENTS:** • It is recommended that EPA OPPT convene a broader discussion with other EPA program offices about how – in the longer term – it should seek to: o better understand the regulatory requirements and processes of the various environmental statutes under EPA's purview; o reach agreement on the value (or not) of EPA's potential use of TSCA risk evaluations to address air, water, and other waste pathways under the TSCA disposal condition of use; and o establish better approaches for coordinating what each program office (including EPA OPPT) can provide the others to improve environmental protection under their respective statutory authorities more efficiently and without duplication.	EPA communicated with other program offices within the agency throughout the assessment process, including at scoping, problem formulation, and risk evaluation. These discussions included regulatory requirements and processes of the various environmental statues. EPA will continue to have these conversations with other offices at the Agency for the next round of chemicals to be evaluated under TSCA Section 6. See section 1.4.2 of the risk evaluation regarding EPA's approach to exposure pathways and risks addressed by other EPA-administered statutes.
67	**PUBLIC COMMENTS:** • The "applicable requirements of TSCA § 6," with which the Lautenberg Act mandates that a completed risk assessment must comply before it can support § 6 rulemaking, include taking into account exposure under the conditions of use,	EPA believes that the MC risk evaluation is sound and has met the requirements of TSCA § 26(h), (i) and (k) to use the best available science in a weight of scientific evidence approach using reasonably available information.

	describing the weight of the scientific evidence for the identified hazard and exposure, using scientific information employed in a manner consistent with the best available science, considering variability and uncertainty in the information, and ensuring independent verification or peer review of the information. • The draft risk evaluation is more of a screening level assessment. Its hazard assessment is not based on the best available science; it uses "strength of evidence" as opposed to "weight of evidence;" its exposure assessment is mostly based on workplace limits in effect 20 years ago that were 20 times higher than current limits; it ignores available EPA data; and it includes no formal or informal uncertainty analysis. To maintain the credibility of its regulatory efforts under TSCA, it is imperative that EPA build upon available information to construct a more realistic risk assessment before proceeding with rulemaking.	

Overall Content and Organization		
EPA's Final Rule, Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act (82 FR 33726) stipulates the process by which EPA is to complete risk evaluations under the Frank R. Lautenberg Chemical Safety for the 21st Century Act. As part of this draft risk evaluation for methylene chloride, EPA evaluated potential environmental, occupational and consumer exposures. The evaluation considered reasonably available information, including manufacture, use, and release information, and physical chemical characteristics. It is important that the information presented in the risk evaluation and accompanying documents is clear and concise and describes the process in a scientifically credible manner. **Charge Question 7.1.** Please comment on the overall quality and relevance of the resources used in this draft risk evaluation; describe data sources or models that could improve the risk evaluation. **Charge Question 7.2.** Please comment on the overall content, organization, and presentation of the draft risk evaluation of methylene chloride. **Charge Question 7.3.** Please provide suggestions for improving the clarity of the information presented in the documents.		
#	**Summary of Comments for Specific Issues Related to Charge Question 7**	**EPA/OPPT Response**

Organization and clarity of presentation		
SACC, 68	**SACC COMMENTS:** • Committee members requested more clarity about the rationale for choices that influence the risk evaluation, and clearer presentation of assumptions. **PUBLIC COMMENTS:** • Increased clarity is requested in the presentation of supporting data and analyses supporting the risk characterization and risk determination.	EPA has added more information to the uncertainties sections and more explanation and detail to the risk characterization section.
SACC	**SACC COMMENTS:** • Committee members suggested EPA standardize first- and second-level headings for the risk evaluations and provide a subsection at the beginning of each section to summarize that section, as well as conclusion sentences. • The use of additional summary graphics was suggested. • One Committee member suggested organizing the report to present information about consumer exposure for each COU and after that to present information about bystander exposure for each consumer COU.	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.
SACC	**SACC COMMENTS:** • Committee members suggested modifying links to external documents as well as internal links within the document to increase transparency. • Some Committee members stated that the risk evaluation should concisely summarize information taken from external documents, rather than only providing links, while other Committee members requested additional links to external supporting materials to improve readability and shorten the risk evaluation.	EPA made an effort to include more summaries of information referenced in other documents. This comment will also be considered in future risk evaluations.
SACC	**SACC COMMENTS:**	A regulatory history of MC is included in Appendix A of the draft and final risk evaluation.

	• A short summary of MC's regulatory status under EPA, OSHA, and FDA should be included.	
66	**PUBLIC COMMENTS:** • Details of the human health hazards section were not clear until the data summary. It is suggested that an introductory paragraph be added that provides an outline and sets up the flow of the section. • EPA could also give a brief overview of the quality rating criteria in this section.	EPA has revised parts of the human health hazard section for better clarity based on other comments. EPA is developing an updated template for future TSCA risk evaluations.
73, 68	**PUBLIC COMMENTS:** • EPA's risk determinations in Table 5-1 do not accurately incorporate the risk estimates from Chapter 4. • In general, Table 5-1 is lacking organization and clarity. For example, some risk estimates are presented only for medium intensity users, while others are presented for high intensity users, without an explanation. • EPA should consider including a modified table (e.g., use of boldface for "presents" and "does not present", color-coding of endpoints that exceed benchmarks, citation to regulatory requirements).	EPA has updated the unreasonable risk determination format for increased clarity regarding the unreasonable risk determination and the risk considerations for each condition of use.
68	**PUBLIC COMMENTS:** • EPA should consider using Health and Environmental Sciences Institute's (HESI's) Risk21 Project and Web Tool application to create a plot of exposure and toxicity data, overlaying a risk matrix represented as a heat map.	EPA will investigate the methods and principles behind the HESI Risk 21 application and consider using its visualizations in future risk evaluations.
66	**PUBLIC COMMENTS:** Clarification is requested for the following: • pp. 65-66: The "other" category of facilities failing to report a NAICS or SIC code is unclear. • Table 2-28, p. 114: It is unclear which central tendency was used. • p. 218: Were there 2878 people who participated or	Regarding the "other" category discussion in section 2.2.1 on pages 65-66, the discussion did not indicate that these facilities failed to report NAICS or SIC codes. The discussion indicates that EPA cannot map the codes reported by these facilities to a specific occupational exposure scenario or condition of use.

	did 2878 people have levels below detection? • p. 226: Does use of menthol refer to menthol cigarettes? • Table 3-12, p. 256: No explanation is provided for downgrading Gold et al. from a high to medium rating. • p. 425: It is not clear what is meant by determining cancer risk "based on other benchmarks as appropriate". • Section 2.4.2: Further explanation of the use of "default parameters" is requested. • Sections 4.2 and 4.3 and tables in Sections 4.2, 4.3, 4.6, and 5: Increased transparency is required. • Section 5: Confidence ratings are presented without any discussion. The origin of these ratings is unclear.	The 8-hr TWA exposure concentration from Table 2-28 was used to calculate risk, which is made clear in the risk characterization section. The 2878 individuals were those who participated and who had their blood monitored for methylene chloride; methylene chloride was not detected in the blood of this sample. Menthol was used only to disguise the odor of MC in a human experimental study (Gamberale et al., 1975), as stated in the human health hazard section of the risk evaluation. EPA added the explanation for downgrading Gold et al. (2010) to Table 3-12. Confidence ratings are explained earlier in the document, and the final version of the document does not list confidence ratings in Section 5.
66	**PUBLIC COMMENTS:** • The sensitivity analysis (p. 179) should be made available to readers.	The CEM sensitivity analysis is available to the public and referenced in the MC RE. It is also available in Appendix C at the following link. https://www.epa.gov/sites/production/files/2017-06/documents/cem_user_guide_appendices.pdf
Addition of Globally Harmonized System (GHS) classification information		
SACC	**SACC COMMENTS:** • One committee member suggested including GHS classification information on the subject chemical.	EPA did not locate any existing U.S. GHS classifications for methylene chloride. EPA doesn't rely on GHS for labelling chemicals under TSCA and therefore has also not separately classified methylene chloride based on the results of this risk evaluation.
Addition of OSHA and/or NIOSH representatives to SACC		
SACC	**SACC COMMENTS:** • Consider adding representatives from OSHA and/or NIOSH to the SACC since many of the COUs are worker exposures.	OSHA and NIOSH were able to comment on this document during interagency review. EPA will consider adding representatives from OSHA or NIOSH to the SACC.
Number of significant digits		

SACC	**SACC COMMENTS:** • Tables in the evaluation should consistently use two significant digits.	EPA has recalculated values with a consistent method for applying significant figures. Results are presented to at least 2 significant digits, with numbers >10 generally reported to the nearest whole integer.
Insufficient time to review		
49, 57, 43, 41	**PUBLIC COMMENTS:** • Insufficient time was allowed for the public to review the draft risk evaluation prior to the SACC meeting. • SACC meetings should be scheduled after the close of the comment period to enable a more informed review.	EPA will consider this comment for future risk evaluations.
Comments related to the 2017 proposed ban on MC		
SACC	**SACC COMMENTS:** • The first mention of the new rule on MC in residential paint strippers in Section 1.4.1 appears too late in the evaluation. Also, this paragraph has descriptions of COUs that are not consistent with the problem formulation.	EPA's regulation prohibiting MC for consumer paint and coating removal is mentioned in the executive summary and then Section 1.4.1. EPA maintains that these are reasonable locations. The conditions of use the reviewer noted ("metal products not covered elsewhere, apparel and footwear care products, and laundry and dishwashing products") are listed because they were identified in the problem formulation and, after additional analysis to further understand the COU (e.g., SDS, literature, industry engagement), EPA found no applicable consumer products for these uses. EPA has determined that there is no known, intended, or reasonably foreseen consumer use of these products. There are only industrial and commercial uses of methylene chloride for these conditions of use, and these conditions of use were assessed.
55, 49, 33, 73, 54, 44, 69, 77, 72, 71, 75, 64, 48	**PUBLIC COMMENTS:** • In 2017, EPA proposed banning the use of MC chemicals in paint strippers. • Earlier this year, EPA finalized a ban on consumer sales and uses of MC in paint strippers, but did not implement a commercial ban, leaving workers and others at risk.	Regulatory actions to address unreasonable risks are outside the scope of this risk evaluation.

	• EPA has not presented an adequate justification for excluding commercial paint stripping uses from the ban. Since 2009, a REACH Restriction entered into force regarding the use of MC in paint strippers, effectively prohibiting the use of MC in such applications. • In the absence of a regulatory backstop from EPA, there is a concern that industry will fail to make a meaningful investment in less toxic alternatives to MC. • Commenters urge EPA to move forward to finalize a ban on commercial paint stripping uses.	
Overall ban of MC in occupational scenarios		
69	**PUBLIC COMMENTS:** • Research on methylene chloride fatalities finds current policies inadequate to protect workers and recommends elimination of methylene chloride use in commercial settings. • The number of fatalities per year did not appear to be reduced by CPSC's 1987 mandatory labelling requirement and OHSA's updated standard in 1997. • The most effective next step is to institute an elimination of methylene chloride in occupational scenarios to prevent further fatalities.	The Risk Evaluation for methylene chloride describes the risk to workers for the conditions of use in scope of the risk evaluation. Regulatory actions to address unreasonable risks are outside the scope of this risk evaluation.
Need to consider environmental and human health effects mediated by ozone depletion		
SACC, 49, 62, 75	**SACC COMMENTS:** • The impact of MC emissions to the atmosphere on ozone depletion should be considered in the evaluation. **PUBLIC COMMENTS:** • MC is an ozone-depleting substance. According to a 2017 study in Nature Communications, rising MC emissions alone could delay the recovery of the ozone layer by 5-30 years, undermining the progress made under the Montreal Protocol.	Assessing ozone depletion is out of scope for this Risk Evaluation. EPA did not include the emission pathways to ambient air from commercial and industrial stationary sources, because stationary source releases of methylene chloride to ambient air are managed under the jurisdiction of Section 112 of the Clean Air Act (CAA). Resulting exposure were out of scope as described in the problem formulation for MC.

	• EPA ignores ozone-depleting effects in its draft risk evaluation. Ozone depletion presents both risks to the environment and human health. • EPA cannot claim that MC's ozone-depleting effects are adequately addressed by the CAA, since EPA has not regulated MC under Title VI of the CAA. • More than 2.5 million pounds of MC are emitted to the air each year. Global emissions of MC are increasing rapidly. • TSCA should be utilized to assess new concerns that are unaddressed by the limited regulatory scope of CAA Title VI.	
General issues with TSCA systematic review		
73, 49, 58, 69, 71, 75	**PUBLIC COMMENTS:** • A protocol describing the methods for the systematic review should be published and peer-reviewed prior to commencing the review. • A protocol should pre-define search terms, search strategy, inclusion/exclusion criteria, and procedures for study selection. The protocol should address specific questions that are identified in the problem formulation. • OPPT should consult with the IRIS program on how to best develop a protocol in consideration of requirements under TSCA. • EPA should include protocols for all systematic reviews conducted for a specific risk assessment as appendixes to the assessment. • Any changes made after the protocol is in place should be transparent, and the rationale for each should be stated.	As described in Section 3.4 of the *Application of Systematic Review in TSCA Risk Evaluations*, TSCA requirements and the results of scoping/problem formulation (i.e., conceptual model(s), analysis plan) framed the specific scientific risk assessment questions to be addressed in each of the first 10 TSCA risk evaluations. The timeframe for development of the TSCA Scope documents was very compressed and the first ten chemical substances were not subject to prioritization, the process through which EPA expects to collect and screen much of the relevant information about chemical substances. As a result, EPA had limited ability to develop a protocol upfront. For these reasons, the protocol development was staged in phases while conducting the assessment work (see Section 3.1 of the *Application of Systematic Review in TSCA Risk Evaluations* for more discussion of this step). EPA published the *Strategy for Conducting Literature Searches for Methylene Chloride* in June 2017 along with the scope document for MC, similar to all 10 first TSCA chemical risk evaluations. This document outlined the literature search strategy and title/abstract inclusion/exclusion criteria used for screening, found in Appendix E.

		Along with publishing the problem formulation for MC in May 2018, EPA published the inclusion/exclusion criteria statements used during full text screening for each chemical in appendices to those documents as well as a separate document titled *Application of Systematic Review in TSCA Risk Evaluations* that described the data quality criteria used for each discipline and outlined data integration strategies that will be further developed for the next risk evaluations. Because the systematic review steps have been published and are available to the public, EPA did not publish the protocols in the risk evaluation documents. EPA has identified within the MC risk evaluation document where changes were made, such as evaluations of additional studies that were not part of the original systematic review process. EPA consulted extensively with the IRIS program when developing the systematic review process and has continued to engage with the IRIS program. EPA plans to publish a protocol document for the next TSCA chemicals undergoing risk evaluation. Furthermore, EPA anticipates feedback from the NASEM TSCA Committee on its systematic review process and will carefully review their recommendations.
49, 57, 43, 58, 68, 75	**PUBLIC COMMENTS:** • There are consistent problems in both the design and implementation of the systematic review system: • EPA should describe efforts undertaken to calibrate the reviews of different reviewers both within and across chemicals, as some inconsistencies in data quality evaluation remain. • The SACC has previously noted a high fraction of studies where the initial quality score was later changed, indicating that the data quality 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

	protocol is not clearly defined and possibly inconsistently implemented by different reviewers. • Other concerns included the need for 'backward reference searching' or 'targeted supplemental searches,' suggesting that the initial search did not find all the relevant references, and that the automated gray literature search found mostly off-topic documents and missed other useful documents. • The draft guidance should be peer reviewed and revised in accordance with the feedback received.	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.
58, 69, 71, 75	**PUBLIC COMMENTS:** • Numerical scores falsely imply a relationship between scores and effect or association. • This system could result in many studies being arbitrarily classified as "poor" or "unacceptable" based on a small number of reporting or methodology limitations that do not negate their overall value for assessing health and environmental risks. • Instead of numeric scoring, EPA should assess risk of bias and quality of individual studies and then, separately, determine certainty in the body of evidence.	As stated in Appendix A of *Application of Systematic Review in TSCA Risk Evaluations*, EPA's goal in using the numerical scoring system is to provide consistency and transparency to the process of evaluating chemicals risks while simultaneously meeting the science standards under TSCA Section 26 (h). The scores were not designed and should not be interpreted as implying any association with effect; they are strictly used to evaluate metrics important to understanding the quality of the studies and data used in the TSCA risk assessments, irrespective of the results of a study. The chosen metrics were informed by previous systematic review frameworks and professional scientific judgment. The system is designed to independently score individual metrics; low scores for the individual metrics would not result in an overall low score unless a certain number of metrics receive low scores. However, a study or data source could be considered unacceptable based on a serious flaw in a single metric. EPA implemented this option because there are criteria associated with individual metrics (e.g., lack of a negative control group) that make a study or data source unusable. Situations that would result in unacceptable ratings are identified a priori in Appendices B through H of *Application of Systematic Review in TSCA Risk Evaluations.* EPA is reviewing its data quality criteria and will publish a protocol document for the next TSCA risk evaluations. In addition, EPA anticipates feedback from the NASEM TSCA Committee, who will review EPA's systematic review process under TSCA. EPA will consider revisions to its approach based on these activities.

68	**PUBLIC COMMENTS:** • EPA should provide a description of the specific studies that were evaluated or screened out, along with a rationale behind the decision to include or exclude.	In June 2017, EPA provided a full bibliography of MC studies that were included and excluded during the title/abstract screening process along with a strategy document describing the literature process and inclusion/exclusion criteria. Also, in the draft risk evaluation document, EPA provided data quality evaluation scores and comments explaining the scores for individual metrics. This was done for both acceptable and unacceptable studies. These scores and comments are provided in multiple supplemental files published with the draft risk evaluation and will also be available with the final risk evaluation.
58	**PUBLIC COMMENTS:** • EPA has not justified removal of the SACC charge question on systematic review for MC that is in other risk assessments. • Previously outlined systematic review issues have not been resolved in this draft risk evaluation.	EPA has received comments on the TSCA risk evaluation process following SACC review of previous draft risk evaluations and anticipates feedback from the NASEM TSCA Committee. EPA determined it was not necessary to receive feedback for systematic review for each chemical individually.
Failure to follow the TSCA systematic review guidelines that are in place		
49, 58, 69, 68, 71, 75	**PUBLIC COMMENTS:** • EPA's draft risk evaluation strays from EPA's systematic review guidance by relying primarily on "key and supporting" information. This phrase is subjective and is not adequately defined. • Although it is apparent EPA made the decision to leverage the literature published in previous assessments to identify "key and supporting" information, a justification and rationale for this decision were not provided.	EPA has revised its searching and screening procedures to include all studies in the systematic review process (screening, data evaluation) for the next set of TSCA chemical risk evaluations. EPA also added additional justification to the risk evaluation for MC.
49, 58, 69, 68, 71, 75	**PUBLIC COMMENTS:** • EPA's "hierarchy of preferences" approach is not peer-reviewed and is used to exclude "acceptable" sources of data. • This approach led to the exclusion of almost 100 studies on environmental release and occupational	Different lines of evidence are routinely used in TSCA chemical assessments because of data availability, sources, underlying documentation, and quality varies. EPA preferentially relies on a variety of test and analog data. In the absence of suitable test data, predictive modeling tools may be used. For environmental hazards, if the modeling tools

	exposure without adequate justification. There is a lack of clarity on how EPA chose and evaluated the 22 remaining key sources that were taken forward to data extraction and evaluation. • The risk evaluation does not provide transparency or rationale for how studies are scored or why they are included or excluded. These methodologies may result in a biased evidence base used to make decisions on hazard endpoints, resulting in the potential for some endpoints (such as immunotoxicity and reproductive/developmental toxicity) to be underestimated or excluded.	cannot provide predictions to an endpoint of interest, then calculations like acute-to-chronic ratios can be used to fill in data gaps. For releases and occupational exposures, the hierarchy of preferences and its use are described in Appendix G of the Supplemental Information on Releases and Occupational Exposure Assessment. The determination of the use of data for each OES are described in Appendix A of the Supplemental Information on Releases and Occupational Exposure Assessment, and this determination illustrates the use of the hierarchy in data decisions for these types of data. EPA published the title/abstract inclusion/exclusion criteria for methylene chloride in Appendix E of the *Strategy for Conducting Literature Searches for Methylene Chloride* and inclusion/exclusion criteria statements used during full text screening in an appendix to the problem formulation document for methylene chloride. Data quality criteria used for scoring each discipline are provided in a separate document titled *Application of Systematic Review in TSCA Risk Evaluations,* which also outlines evidence integration strategies that will be further developed for the next risk evaluations. EPA consulted multiple systematic review frameworks and the IRIS program when developing the systematic review process. EPA is reviewing its data quality criteria and will publish a protocol document for the next TSCA risk evaluations. In addition, EPA anticipates feedback from the NASEM TSCA Committee, who will review EPA's systematic review process under TSCA. EPA will consider revisions to its approach based on these activities.

Use of guideline studies		
55, 69	**PUBLIC COMMENTS:** • According to TSCA systematic review, higher quality studies are guideline studies or data collected according to Good Laboratory Practices (GLP) requirements. • This results in inappropriately favoring industry studies and can lead to a biased evidence base that favors no-effect findings.	The TSCA risk evaluation strategies in some cases refer to study guidelines along with professional judgement as helpful guidance in determining the adequacy or appropriateness of certain study designs or analytical methods. This should not be construed to imply that non-guideline studies are automatically given lower confidence ratings than guideline or Good Laboratory Practice (GLP) studies. EPA considers reasonably available, relevant data and information that conform to the TSCA science standards when developing the risk evaluations irrespective of whether they were conducted in accordance with standardized methods (e.g., OECD test guidelines or GLP standards).
55	**PUBLIC COMMENTS:** • Industry-sponsored guideline studies that are submitted for the purposes of regulatory approval are not sufficiently sensitive and may underestimate risks. • Guideline studies focus on major (apical) toxic effects and are not designed to deal with the issues of low-dose exposures, endocrine or hormonal effects, and subtle but significant neurobehavioral impacts, and therefore may not identify upstream indicators of potential harm.	EPA considered reasonably available, relevant data and information that conform to the TSCA science standards when developing the risk evaluation. Recognizing that each source of data may have strengths and weaknesses, EPA considered data quality and relevance and then used acceptable data in a weight of the scientific evidence approach. Furthermore, EPA will consider data and information from alternative test methods and strategies (or new approach methodologies or NAMs), as applicable and available, to support TSCA risk evaluations. This is consistent with EPA/OPPT's *Strategic Plan to Promote the Development and Implementation of Alternative Test Methods (Draft)* to reduce, refine or replace vertebrate animal testing (U.S. EPA, 2018e). Since these NAMs may support the analyses for the exposure and hazard assessments, the data/information quality criteria may need to be optimized or new criteria may need to be developed as part of evaluating and integrating NAMs in the TSCA risk evaluation process.
Other systematic review platforms to be considered		

73, 58, 69, 71, 75, 55	**PUBLIC COMMENTS:** • While the NAS review is progressing, OCSPP should adopt one of the recognized systematic review methodologies endorsed by the NAS and other peer review bodies. Established systematic review methods include NTP's Office Health Assessment and Translation (OHAT) method, the EPA IRIS method, the Navigation Guide used by the WHO, and Woodruff and Sutton (2014). • The EPA TSCA program should consider incorporating scientific approaches from the systematic evidence-based method recently published in Nature Reviews Endocrinology.	EPA consulted multiple systematic review frameworks when developing the systematic review process for the first 10 TSCA risk evaluations. For any future revisions, EPA will wait to receive feedback from the NASEM TSCA Committee before adopting other published systematic review methods.
Data quality criteria: inconsistencies and the impact on epidemiological studies		
73, 69, 71, 75	**PUBLIC COMMENTS:** • EPA has downplayed or dismissed epidemiological evidence using unsupported or misleading arguments. • OPPT's updated data quality criteria for epidemiological studies are flawed and biased and do not represent best practice. • Certain revisions to these criteria make it more difficult for epidemiological studies to be scored overall as high quality. Epidemiological studies are thus less likely to be considered high quality overall and as a result may be given more limited consideration than animal and in vitro studies. • The scheme used to calculate the overall rating for a particular study is not clearly presented. • OPPT needs to provide explanation or empirical support for its revisions to the data quality criteria for epidemiological studies. • EPA should consider other study evaluation tools that are more appropriate for the consideration of the quality of observational epidemiologic studies, such as the Conducting Systematic Reviews and	EPA has comprehensively evaluated the human and animal studies for MC. Although many epidemiological studies may have been conducted adequately, there are still inherent aspects of some of these studies (such as lack of control for co-exposure to other chemicals that are associated with the same outcome), which make it difficult to either fully understand the true relationship between MC and cancer or use the studies quantitatively in a risk evaluation. However, EPA clearly identified relevant issues and described the logic regarding which endpoints and studies would be considered for dose-response in the weight of scientific evidence section. 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

	Meta-Analyses of Observational Studies of Etiology (COSMOS-E) tool (Dekkers, Vandenbroucke et al., 2019) and the Navigation Guide (Woodruff and Sutton, 2014).	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 epidemiological 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 for the criteria to represent a more accurate depiction of the quality levels of the epi literature, the criteria were revised using two methods. 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 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. 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.
73	**PUBLIC COMMENTS:** • With the recent announcement that EPA intends to move away from using animals for toxicological testing, EPA should not require evidence from animal studies where significant epidemiological evidence exists. • Well-conducted epidemiological studies are more	EPA has used information consistent with the best available science, as required by TSCA Section 26(h). EPA comprehensively reviewed epidemiological and animal studies as well as mechanistic information. EPA used data from a human experimental study (Putz et al., 1979) to evaluate risks for acute exposure scenarios and uses epidemiological studies to support other endpoints in a weight

	representative of an agent's biological effects on humans and should therefore be able to provide sufficient evidence for decision-making.	of the scientific evidence. Also, the existing database for MC includes numerous animal toxicity studies and hence, it is part of the "best available" information. MC has animal evidence that is reasonably available for most endpoints. EPA used all information reasonably available to assess the hazards of MC, as specified by TSCA Section 26 (k). In cases where EPA requests or requires testing for purposes of TSCA risk evaluations, EPA will comply with the requirements related to reduction of vertebrate testing in TSCA section 4(h).
69	**PUBLIC COMMENTS:** • Concern was expressed regarding the accuracy and consistency of EPA's evaluation of data quality of epidemiology studies. An example was provided in which participant selection was confused with attrition.	EPA designed evaluation criteria that consider risk of bias and Bradford Hill criteria when assessing the quality of epidemiological studies. Refer to Appendices F, G and H of the *Application of Systematic Review in TSCA Risk Evaluations* document for more information. Furthermore, EPA made changes to the epidemiological criteria since the *Application of Systematic Review in TSCA Risk Evaluations* was published. These changes included validation and improvement efforts to ensure that the most relevant studies were included in the TSCA risk evaluations. The most up-to-date data quality evaluation criteria will be available for review in the upcoming the *Systematic Review Protocol Supporting the TSCA Risk Evaluations* document (under development). 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.
75	**PUBLIC COMMENTS:** • EPA should consider addressing limitations that	EPA did consider evidence across all epidemiological studies as well as animal toxicity and mechanistic data (Sections

	are routine in epidemiologic studies (such as small numbers or co-exposure to other carcinogens) by using standard statistical adjustments, considering all the evidence across many studies, and/or considering supporting evidence from animal studies and other streams of evidence. • EPA should consider revising its review and synthesis of the epidemiological evidence to more fully incorporate the strengths and weaknesses of the epidemiological studies and integrate these studies with the available animal and mechanistic evidence to support conclusions regarding carcinogenic hazard.	3.3.3 and 3.3.4). EPA will investigate methods, which may include meta-analyses, for future risk evaluations. EPA comprehensively reviewed the epidemiological evidence and considered the merits and limitations of all studies as described in the weight of scientific evidence section (Section 3.3.4). EPA has added more discussion of individual epidemiological studies and the suite of epidemiological data to the MC risk evaluation (Section 3.3.4).
41, 73	**PUBLIC COMMENTS:** • EPA should develop formal data quality criteria for controlled human exposure studies, considering relevant data quality criteria from available sources.	EPA evaluated the human controlled experiments qualitatively drawing upon the types of metrics identified for both human epidemiological studies and animal studies published in *Application of Systematic Review in TSCA Risk Evaluations*. EPA is also committed to developing criteria for human exposure studies (e.g., experimental studies such as the acute inhalation studies of CNS effects). EPA will also carefully review and implement relevant recommendations of the NASEM TSCA Committee that may pertain to developing such criteria.
Data quality evaluation of in vitro and mechanistic studies		
41, 56, 68	**PUBLIC COMMENTS:** • EPA did not re-evaluate genotoxicity studies for quality but is relying on previous assessments. EPA does not provide a sufficient justification for this decision. • EPA should acknowledge that a formal data quality assessment was not performed on any cited in vitro studies. • In vitro and mechanistic studies that were used as supporting evidence in the development of a proposed MOA should be subject to a formal data	EPA has evaluated the genotoxicity studies for data quality and added more information to the final risk evaluation (Section 3.3.3.2, Genotoxicity and Carcinogenicity; Appendix ; Supplemental File on Evaluation of Animal and In Vitro Studies). Other MOA data were not reviewed. Thank you for your suggestion regarding tiering *in vitro* studies for review. The NASEM TSCA Committee will review EPA's systematic review process, and EPA will consider revisions to the process based on their recommendations.

	quality assessment and the quality should be discussed in the weight of scientific evidence section. • In instances where there are numerous studies, EPA could consider developing a specific tiered approach for evaluating in vitro data quality in which a subset of the full data quality domains deemed critical for each in vitro assay type are considered first, and those studies that do not meet these criteria be considered as low quality.	
Data availability – Handling of CBI data		
73, 49	**PUBLIC COMMENTS:** • Regarding citations for which EPA does not possess full study reports, EPA needs to obtain copies of the full studies and make these available to the public (e.g., through online portals such as HERO), allowing better assessment of data quality and study conclusions. • It is requested that these references be placed in the docket for the draft risk evaluation and that EPA provide an opportunity for public comment on them. • EPA has not provided public access to several sources that include health and safety information on which EPA relies in its draft risk evaluation. These studies cannot receive confidential business information (CBI) protection under TSCA. **PUBLIC COMMENTS:** • Under TSCA Section 14, restrictions on disclosure of CBI do not apply to "any health and safety study which is submitted under this Act" for a chemical substance which "has been offered for commercial distribution". • Any information, including physical-chemical properties, fate, human health effects, ecotoxicity, and exposure assessments, received by EPA on	• 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. • Conditions of use with CBI or unknown function were evaluated and considered for the methylene chloride risk evaluation; however, the non-CBI elements of the category, subcategory, function and industrial sector were used in the analysis as these data were higher quality. This applies to CBI function for petrochemical manufacturing, paint additives and coating additives not described by other codes for CBI industrial sector, laboratory chemicals for CBI industrial sectors, manufacturing of CBI and oil and gas drilling, extraction, and support activities. For Processing as a Reactant, Arkema Inc. submitted data claimed as CBI for a fluorochemicals manufacturing facility. The CBI data were not included in this assessment. Higher quality data from HSIA were used instead.

	such a chemical is not protected as CBI and must be disclosed.	
Comments related to the methods of evidence/data integration		
73, 71, 75, 56, 68, 69	**PUBLIC COMMENTS:** • OPPT has not provided a pre-established methodology for data/evidence integration and does not sufficiently describe its approach. Only general, high-level principles are described, without specific details. • This may lead to bias and inconsistency in how EPA conducts WOE integration across risk evaluations. • EPA should describe its general approach to evidence integration in a revised systematic review methodology document and then incorporate that	When synthesizing and integrating evidence for each human health hazard endpoint, EPA considered quality, consistency, relevancy, coherence and biological plausibility as specified in *Application of Systematic Review in TSCA Risk Evaluations*. EPA used an informal framework for most endpoints but did array the immunological evidence within a more formal framework to respond to a comment by the SACC (see Appendix A below and Appendix M in the risk evaluation). Sections 3.2.3 and 3.3.4 describe EPA's process of weighing and integrating scientific evidence for hazard endpoints.

	into specific protocols it develops for each risk evaluation. This approach should be fit-for-purpose to meet statutory and regulatory requirements and should be subject to review and public comment. • It is recommended that EPA conduct separate evidence synthesis and determinations about the certainty of the evidence for each stream of evidence and describe how different streams of evidence are integrated to reach a conclusion for each health effect. • EPA should follow the recommendations of the NASEM.	EPA is developing and implementing more formal and structured data integration strategies for the next set of TSCA chemical risk evaluations. In addition, EPA anticipates feedback from the NASEM TSCA Committee on its systematic review process and will carefully review and implement relevant recommendations.
Editorial		
SACC, 66	**SACC and PUBLIC COMMENTS:** • The SACC and public comments provided many suggestions for editorial comments that EPA will consider.	EPA considered and revised many of the editorial suggestions and comments provided by the SACC and the public.

Appendix A: Immunotoxicity Evidence Integration

Human: Epidemiological Evidence				
Endpoint	**OR/HR/SMR (95% CI)**	**Important study characteristics**	**Study Confidence Rating**	**Reference**
Mortality from infectious and parasitic diseases	SMR all divisions: 0.0 (0.0-0.66)[a] SMR roll coat: 0.67 (0.14-1.97)[a]	MeCl exposure quantified and duration-adjusted; MeCl was primary exposure for all divs; other chemical exposures possible (not controlled) for roll coat; dissimilar comparison group for all divs;	High	Hearne and Pifer (1999)
Mortality from influenza and	SMR males: 1.25 (N/A)	MeCl exposure quantified; Other	Medium	Gibbs (1992)

pneumonia	SMR females: 4.36 (N/A)	chemical exposures not controlled; dissimilar comparison group		
Mortality from bronchitis (non-specific)	HR: 9.21 (1.03–82.69)	MeCl exposure estimated based on job duties; Other chemical exposures identified (~ 21 solvents) but not controlled	Medium	Radican et al. (2008)
Mortality from non-malignant respiratory disease	SMR: 0.97 (0.42-1.90)	MeCl exposure quantified; methanol and acetone exposure not controlled; dissimilar comparison group	Medium	Lanes et al. (1993)
Sjorgen's Syndrome (autoimmune)	OR: 9.28 (2.60-33.0) 3.04 [cum.] (0.50 – 18.3)	MeCl exposure estimated based on job duties; Other chemical exposures not controlled	Medium	Chaigne et al. (2015)

[a] SMRs reported in study on different scale: SMR all divs = 0 (0 - 66) and SMR roll coat = 67 (14 – 197)

Animal Evidence							
Species	**Exposure Route**	**Doses/ Concentration**	**Duration**	**NOAEL[a]**	**Effect**	**Study Confidence Rating**	**Reference**
Rat, SD	Inhalation	0, 5187 ppm	6 hrs/day, 5 days/wk, 28 days	5187 ppm	No IgM antibody response after sheep RBC injection; Decreased spleen wts (females)	High	Warbrick et al. (2003)
Mouse, CD-1 (female)	Inhalation	0, 52, 95 ppm	3 hrs	52 ppm	Acute: ↑ mortality (12.2%; $p < 0.01$) from *S. zooepidemicus*; ↓ bactericidal activity (12%; $p < 0.001$)	Medium	Aranyi et al. (1986)
		0, 51 ppm	3 hrs/day for 5 days	51 ppm	None re: mortality or bactericidal activity		
Rat, F344	Inhalation	0, 1000, 2000, 4000 ppm	6 hrs/day, 5 days/wk, 2 years	1000 ppm	Splenic fibrosis; no patterns in inflammatory cells in respiratory tract	High	NTP (1986)
Mouse, B6C3F1	Inhalation	0, 2000, 4000 ppm	6 hrs/day, 5 days/wk, 2 years	2000 ppm	Splenic follicular atrophy; no patterns in inflammatory cells in respiratory tract	High	NTP (1986)

Rat, SD	Inhalation	0, 50, 200, 500 ppm	6 hrs/day, 5 days/wk, 2 years	500 ppm	No histopathological or other changes in lymph nodes, thymus or spleens; no patterns in inflammatory cells in respiratory tract	High	Nitschke et al. (1988)
Rats, hamsters	Inhalation	0, 500, 1500, 3500 ppm	6 hrs/day, 5 days/wk, 2 years	3500 ppm	No histopathological or other changes in lymph nodes, thymus or spleens; no patterns in inflammatory cells in respiratory tract	High	Burek et al. (1984)

[a]EPA-derived as related to immune endpoint

Mechanistic Evidence			
System	**Effect**	**Study Confidence Rating**	**Reference**
Male were rats treated with hemin arginate (HAR), which induces heme oxygenase-1 (HO-1). Hemorrhage was then induced in the mice. In part of the experiment, the mice were then treated with a heme oxygenase-1 blocker, and then administered 100	• HAR resulted in ↓ pro-inflammatory cytokine TNF-alpha and ↑ anti-inflammatory cytokine IL-10. • The HO-1 blocker abolished this effect but then administration of methylene chloride restored the anti-inflammatory response.	N/A	Kubulus et al. (2008)

mg/kg-bw methylene chloride.	• The authors suggest that the anti-inflammatory response is partly due to carbon monoxide release from administration of methylene chloride (in addition to the HAR administration/HO-1 induction)		
Evaluation of peripheral blood mononuclear cells in carp after exposure to 0.004-40 mg/kg-bw methylene chloride by i.p.	↑ mitochondrial activity and H2O2 of peripheral blood mononuclear cells in a dose-dependent fashion suggesting an immunomodulary effect related to an acute pro-inflammatory state. Also, ↑ apoptosis and generation of other ROS was observed. Exact immunomodulary effects are unclear.	N/A	Uraga-Tovar et al. (2014)

Evidence Integration Summary Judgment: Immunotoxicity

Summary of Human, Animal, and Mechanistic Evidence

Evidence from Studies of Exposed Humans

Studies, outcomes, and confidence	Factors that increase strength or certainty	Factors that decrease strength or certainty	Key findings and interpretation	Evidence stream summary
• Mortality from infectious disease – SMRs > and < 1 • Autoimmunity – OR > 1 • Mortality from non-specific respiratory disease – SMR/HR > and < 1 • Hearne and Pifer 1999): high confidence; all others: medium confidence • Lack of quantitative methylene chloride air concentration measurements and use of dissimilar comparison groups in most studies, • Lack of control for other chemicals, some of which are solvents and may also be associated with immunotoxicity	• Magnitude of effect Large OR for one of the autoimmunity measurements • One large SMR for morality from bronchitis (but a non-specific effect) • SMRs > 1 for study of mortality from flu/pneumonia (a severe outcome)	• Inconsistency Infectious disease: one SMR > 1 and another is < 1 • Imprecision Lack of information on precision for one study (Gibbs); imprecise association for cum exposure odds ratio for autoimmunity (Chaigne) • Dose-response Insufficient information to judge gradient • Coherence across types of immunity Inconsistency within types of studies and limited study numbers make it difficult to judge coherence	• Mortality from infectious disease: Possible association with methylene chloride but results are inconsistent and outcome is severe (mortality) • Autoimmunity: Possible strong association with methylene chloride but only one study is available • Some study designs may limit ability to discern effects associated specifically with methylene chloride	• Results across human epidemiological studies suggest that methylene chloride may be associated with immunosuppression and autoimmunity • Inconsistencies across studies, severity of outcome (mortality) and limitations of study design preclude firm conclusions • Mechanistic evidence: Support unclear given the limited database

Evidence from In vivo Animal Studies

Studies, outcomes, and confidence	Factors that increase strength or certainty	Factors that decrease strength or certainty	Key findings and interpretation	Evidence stream summary
• Bacterial resistance assay – effect observed • Functional immune (IgM) assay – no effect observed • Clinical chemistry/ histopathology results (multiple studies) – change in histopathology of spleen within some studies • Aranyi et al. 1986):	• Effect size/precision: Bacterial resistance assay showed two statistically-significant possibly related results of similar magnitude • Consistency Several studies showed effects on	• Only a single study of bacterial resistance is available • Burek didn't identify histopathological changes in the spleen at a concentration identified with splenic changes in other studies • Splenic fibrosis showed somewhat	• One study positive for bactericidal activity but limited support • Support from animal studies only includes histopathological changes in the spleen in some studies.	• Limited information based on a single study of bactericidal resistance with some changes in spleens in some studies. However, lack of support from IgM RBC assay • Mechanistic evidence: Support is unclear given the limited

Inferences across evidence streams

- Bacterial resistance and histopathological changes in the spleen are assumed to be relevant to humans
- Some evidence for decreased resistance to infection (bactericidal assay in rats; increased mortality in humans from flu/pneumonia) but lack of support from IgM RBC assay
- Autoimmunity evaluated in only one study
- Effects on spleen common to multiple studies
- Susceptible populations may include people with compromised immune systems and the elderly
- Other solvents have been associated with effects on the immune system

medium confidence; all others: high confidence	spleen (decreased weight, atrophy, fibrosis) • Dose-response gradient – spleen effects observed at higher concentrations	unclear dose-response trend (2%, 10%, 20%, 14% at 0, 1000, 2000 and 4000 ppm) • Two-year studies didn't identify effects on immune cells and organs than the spleen • No increased rates of infection were identified in 13-week and 2-year studies • RBC study to determine IgM response was negative.		database	
Mechanistic Evidence or Supplemental Information					
Biological events or pathways (or other information)	**Species or model systems**	**Key findings, limitations, and interpretation (for each row below)**	**Evidence stream summary**		
• Pro-inflammatory, but somewhat non-specific, changes (one study) • Anti-inflammatory changes (one study)	• Two *in vivo* studies • Rat and carp	The limited number of studies, differences in species, types of cells and substances studied as well as differences in processes evaluated make it difficult to make any conclusions regarding these studies.	Little can be concluded from these two studies that have very different study protocols. It is not clear whether the studies suggest opposite effects or are just two aspects of a coordinated immune response.		

Appendix B: Evaluation of Steep Dose-Response Information for Acute Exposure Endpoint

Most case reports of human deaths lack information on exposure conditions; some that do have such information, however, include a fairly low exposure concentration within that range (100 ppm for 55 minutes and lower). Thus, EPA still considers the possibility that there could be a steep dose-response from more subtle CNS effects up to death in humans.

Winneke (1974) exposed individuals at 300, 500 or 800 ppm methylene chloride in four separate experiments. A more direct comparison between these results and the results from Putz et al. (1979) was attempted by considering them on a scale of increasing methylene chloride concentrations (See Table below). Overall, EPA did not consider measures among Winneke (1974) and Putz et al. (1979) to be similar enough to allow a full assessment of the steepness of any dose response. However, considering the magnitude of responses for the data described by the Winneke (1974) experiments, the results don't provide evidence for a steep dose-response curve. Specifically, the results of both visual and auditory vigilance tests were the same or greater at 300 ppm compared with 500 ppm; the effect at 800 ppm is approximately 2x the effect at 300 and 500 ppm but is still an 8% change.

Visual and Auditory Effects Compared with Controls (3.8 to 4 Hours)

Conc. (ppm)	Visual	Auditory vigilance	Reference
195	36% dec. hand-eye [a] 17% dec. peripheral [a]	17% decrease [b]	Putz et al. (1979)
300 [tests 2 +3]	~ 0.95 decrement in CFF [c]	Omission errors: ~ 4% increase [b]	Winneke (1974)
500 [tests 1 +3]	~ 0.95 decrement in CFF [c]	Omission errors: ~ 3% increase [b]	
800 [test 2]	~ 2.5 decrement in CFF [c]	Omission errors: ~ 8% increase [b]	

[a] Dual task: Eye-hand coordination - participant manipulates a small hand control level to position an oscilloscope beam in the center of a scope face; the participant had to track the forcing function that moved the beam and force it back to center (hence, the eye-hand coordination). The second part of the task was to monitor peripheral stimuli for occurrence of a signal. The participant pressed a response switch to respond to the signal.

[b] **Putz et al. (1979):** Participants listened to a train of white noise pulses. At random intervals (and a probability of 0.20) a slightly less intense or more intense pulse was inserted. The participant had to press a hand-held button when they heard the less intense signal. The measure reported here is percent of correct detections, not including responses when no signal was sent out). All tests were automated using a laboratory digital computer. **Winneke (1974):** A similar test was used, but with slight differences. Probability was 0.03 and only less intense pulses were used. Response was omission errors, or percent of signals missed per 15 minutes. Although the methods are similar, it is not clear that the outcome measures are comparable. However, if they are comparable, then the magnitude difference compared with controls was greater at a lower concentration and appears to show an inverse dose-response. No information on automation.

c – Critical flicker frequency was determined using an electronic flicker device, brightness of flicker light and with the on-off ratio held constant. Descending presentation was employed, although it is not clear what this means. The result is an average of 8 single descending CFF determinations

EPA also investigated the presence of a dose-response relationship at 2 hours. EPA compared reaction time information between Gamberale et al. (1975) and Divincenzo et al. (1972). Although these studies both received low data quality evaluations, reaction time changes were not observed at concentrations of 100 and 200 ppm (Divincenzo et al., 1972) and up to 750 ppm (Gamberale et al., 1975), but changes were seen at 1000 ppm (Gamberale et al., 1975). These comparisons do not provide enough information on the steepness of the dose-response curve because changes were observed only at the highest concentration.

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