



Environmental Defense Fund
Comments for Toxic Substances Control Act (TSCA)
Science Advisory Committee on Chemicals Review of
the Draft Risk Evaluation of Methylene Chloride
Docket ID: EPA-HQ-OPPT-2019-0437

Submitted November 26, 2019

Environmental Defense Fund (EDF) appreciates the opportunity to provide comments on the Environmental Protection Agency's (EPA) draft risk evaluation for methylene chloride being prepared under section 6(b)(4) of the Toxic Substances Control Act (TSCA) as amended by the Lautenberg Act, enacted on June 22, 2016.¹

These comments are being submitted by EDF to assist the TSCA Scientific Advisory Committee on Chemicals (SACC) in its peer review of the draft risk evaluation for methylene chloride. They have been prepared in the few weeks provided by EPA to submit comments for consideration by the SACC. EDF will also be providing oral comments at the SACC meeting scheduled for December 3-4, 2019. EDF reserves the right to supplement these comments at the SACC meeting and to provide additional comments on the risk evaluations on or before the comment period deadline of December 30, 2019. We request that these comments be immediately provided to the SACC for its review and consideration.

Summary

In its draft risk evaluation for methylene chloride, EPA has grossly understated the risks from exposure to the chemical. EPA did more frequently identify unreasonable risks than in draft risk evaluations for other chemicals released in the past year, making the deficiencies harder to discern. But EPA has employed a host of unwarranted and unsupported assumptions and methodological approaches that lead it to either avoid identifying unreasonable risk when it should have, or to understate the extent and magnitude of the unreasonable risks it did identify. Below we summarize some of the major concerns addressed in these comments.

¹ U.S. EPA, *Draft Risk Evaluation for Methylene Chloride CASRN: 79-05-2* (October 2019), <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0437-0023>. Further citations in these comments of the draft risk evaluation consist of only a page number in parentheses.

Underestimation of occupational risks: Of particular concern is the extent to which EPA has underestimated occupational risks. EDF has conducted extensive analyses of each of the hundreds of individual risk estimates EPA has made in this draft risk evaluation, which are presented in sections 5.A., 5.B., and 9.A. of these comments. EDF's analyses identify and quantify five major ways in which EPA has underestimated occupational risks, including through: its unsupported assumptions regarding worker use of personal protective equipment in many scenarios; its use of a cancer risk benchmark level for workers that fails to protect them as a vulnerable subpopulation as required by TSCA; its failure to consider combined exposures of workers from multiple sources; its failure to identify unreasonable risks for the most highly exposed, and hence most vulnerable, of occupational non-users (ONUs); and dismissal of numerous unreasonable risk findings by invoking "uncertainty" or unwarranted use of PPE, or without any explanation at all. See section 9.A.v. of these comments.

Exclusion of known uses and exposures: Once again, EPA has abdicated its responsibility under TSCA to identify and evaluate the risks the chemical presents to the general population, by excluding from its risk evaluation conditions of use and exposures that are known or reasonably foreseen, including exposures from releases of methylene chloride to air, water, and land. See section 2 of these comments.

Insufficient consideration of vulnerable subpopulations: EPA has not met its mandatory duty under TSCA to thoroughly identify and evaluate the risks to vulnerable subpopulations. These include subpopulations that are genetically susceptible to methylene chloride exposure; the developing fetus who may be exposed through placental transfer of the chemical; and consumers and others who may be at risk of cancer from acute exposures. See section 1.A. of these comments.

Dismissal of epidemiological evidence: EPA has sought to downplay or dismiss epidemiological evidence through a series of unsupported, misleading arguments and the application of flawed, biased systematic review criteria that do not represent best practice. See section 6 of these comments.

Failure to appropriately account for uncertainty: EPA has neither acknowledged nor addressed the major uncertainties in the available hazard data, including by not applying or by underestimating the necessary uncertainty factors when deriving its benchmark risk values. Ironically, EPA invokes uncertainty as an unwarranted basis for ignoring risks it has identified to the environment and to ONUs, and for not accounting for combined exposures to methylene chloride. See sections 4.D, 4.E, 4.F., and 8.A. of these comments.

Failure to use its authority to address data gaps and uncertainties: Even as it invokes lack of data and uncertainty as reasons to avoid finding risks, EPA has utterly failed to utilize the enhanced

authorities Congress granted it in 2016 to ensure that it has or obtains robust information on methylene chloride’s uses, hazards and exposures. See sections 7.B. and 8 of these comments.

These comments first provide some broad, cross-cutting concerns about the draft risk evaluation as a whole and then present additional comments in the approximate order of the scoping, risk evaluation and risk determination processes. The order of the comments does not imply relative importance.

Table of Contents

1. Broad/cross-cutting concerns.....	6
A. EPA has given insufficient consideration to vulnerable subpopulations.....	6
B. EPA has overrelied on personal protective equipment and the adequacy of OSHA requirements.....	7
C. EPA’s draft risk evaluation suffers from a lack of transparency.	11
i. <i>EPA must obtain and make public the full studies on which it relies.</i>	11
ii. <i>EPA’s risk evaluation lacks an adequate mass balance.</i>	13
D. The SACC must address the scientific consequences of EPA’s “policy” determinations.....	14
2. EPA has inappropriately or illegally excluded conditions of use and exposures.	16
A. EPA failed to analyze certain reasonably foreseen conditions of use.	16
B. EPA has inappropriately excluded exposures based on other statutes.	17
C. EPA needs to analyze those potentially exposed or susceptible subpopulations that face greater exposure due to their proximity to conditions of use.....	19
D. EPA excluded a number of workplace-related exposure scenarios.....	20
3. EPA must adopt a linear, no-threshold approach for methylene chloride’s carcinogenicity.....	22
A. There is strong support for methylene chloride’s cancer classification and a mutagenic mode of action.....	22
B. The scientifically sound and health-protective approach is to use linear extrapolation in cancer dose-response modeling for methylene chloride.....	24
i. <i>Justification based on existing guidance</i>	24
ii. <i>Justification based on human population variability and other real-world considerations to protect public health</i>	24
4. EPA’s human health hazard assessment raises significant questions and concerns.....	26
A. EPA fails to acknowledge that methylene chloride has the potential to transfer through the placenta to a developing fetus.	26
B. EPA has failed to include any estimate of acute cancer risks.....	27

C. EPA’s calculations of inhalation unit risk (IUR) for cancer are flawed and lack transparency.	28
i. EPA’s IUR calculation gives insufficient consideration to susceptible subpopulations.	28
ii. EPA’s IUR calculations lack transparency.	29
a. Modeling based on Aiso et al. 2014.....	29
b. Deviation from Bayesian modeling approaches.....	30
c. Selection of whole-body dose metric.....	31
d. Overall differences from previously derived hazard values	31
e. Classification of liver foci as “non-neoplastic”	31
D. EPA’s modeling decisions for acute non-cancer central nervous system (CNS) effects lack sufficient justification.....	32
i. Derivation of points of departure (PODs).....	32
ii. LOAEC to NOAEC uncertainty factor.....	33
E. EPA’s modeling decisions for chronic non-cancer effects are not sufficiently protective of public health.	34
i. EPA fails to include a necessary database deficiency uncertainty factor (UF) for chronic non-cancer liver effects.....	34
ii. EPA’s decision to ignore human evidence of hematologic effects results in a less protective risk metric.	35
F. EPA fails to include all necessary uncertainty factors in calculating the benchmark margins of exposure, resulting in inaccurate risk characterizations.	36
G. EPA should migrate to a unified approach to presenting dose-specific population risks for both cancer and noncancer endpoints.	36
5. EPA’s human exposure assessment raises significant questions and concerns.	37
A. EPA’s unwarranted assumption of respirator use obscures the full extent of unreasonable risk to workers posed by inhalation of methylene chloride.	37
i. Context and summary	37
ii. Detailed analysis of COUs where EPA assumed routine use of respirators.....	39
B. EPA’s unwarranted assumption of glove use obscures the full extent of unreasonable risk to workers posed by dermal exposure to methylene chloride.....	48
C. EPA has underestimated occupational and consumer exposures.	49
i. EPA has failed to consider workers’ combined exposure from multiple pathways.	49
ii. EPA may have underestimated exposure to ONUs.....	50
iii. EPA has failed to explain or justify its assumption of one exposure event per day.....	51
iv. EPA’s assessment of dermal exposure likely underestimates exposure due to its crude assumptions about glove use and efficacy.	51

D.	EPA inappropriately relies solely on occupational exposure data from the Halogenated Solvents Industry Alliance for two conditions of use and ignores available data from OSHA to support its determinations of no unreasonable risk.....	53
E.	EPA inappropriately characterizes and relies on the OSHA Permissible Exposure Limit.....	55
F.	EPA did not rely on either an aggregate or sentinel exposure assessment.	56
	<i>i. EPA did not perform an aggregate exposure assessment.....</i>	57
	<i>ii. 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.....</i>	58
6.	EPA inappropriately dismisses or downgrades epidemiological data.	59
A.	EPA dismisses human epidemiological studies and disregards their well-accepted value in public health risk assessment	59
B.	EPA’s approach to and application of systematic review data quality criteria suggest bias and are inconsistent.	61
	<i>i. OPPT provides neither explanation nor empirical support for its revisions to the systematic review data quality criteria for epidemiological studies, which make it difficult for epidemiological studies to be scored as overall as high quality.</i>	61
	<i>ii. EPA’s application of the OPPT tool lacks a consistent framework: an illustrative example.....</i>	62
7.	EPA’s environmental assessment raises a number of questions and concerns.....	64
A.	EPA cannot ignore environmental releases of a chemical because it cannot attribute each release to a particular condition of use.....	64
B.	EPA has failed to adequately address risks to terrestrial organisms.....	64
C.	EPA’s analysis of aquatic risks may underestimate the risk.....	67
8.	EPA’s draft risk evaluation suffers from major data gaps and associated analytical inadequacies.....	68
A.	EPA needs to apply an uncertainty factor (UF) to account for lack of dermal toxicity data.....	68
B.	EPA has made inappropriate assumptions about activity rates in its route-to-route extrapolation for dermal PODs.	68
C.	EPA lacks crucial developmental neurotoxicity data.	69
9.	EPA’s unreasonable risk definition and risk determinations are severely flawed.....	70
A.	EPA grossly underestimates occupational risk, leading to ‘no unreasonable risk’ findings or understatements of the extent and magnitude of the unreasonable risks it does find.....	70
	<i>i. By assuming use of PPE, EPA conflates risk evaluation and risk management and significantly understates risk.</i>	70

ii. EPA’s use of a 1 in 10,000 cancer risk level as reasonable for workers is deeply flawed.	71
a. EPA’s approach must be rejected on scientific as well as legal grounds.	71
b. EPA’s approach leads to a massive understatement of the extent to which workers and ONUs face unreasonable risk from methylene chloride exposure.	73
iii. In nearly a third of its risk determinations, EPA inappropriately fails to find unreasonable risk despite exceedances of its benchmarks for high-end exposures.	75
iv. EPA shifts the goalposts when risk values are only a little below – but not above – its benchmark MOEs.	77
v. EPA has dismissed numerous unreasonable risk findings by invoking “uncertainty” or without any explanation at all.	78
a. Dismissal of unreasonable risk based on “uncertainty”	78
b. Dismissal of unreasonable risk by invoking unwarranted use of PPE or without any explanation.	79
B. EPA cannot reasonably dismiss its findings of environmental risk merely by invoking uncertainty.	80
C. EPA failed to analyze distribution in commerce and made unsupported risk findings about this condition of use without a supporting analysis.	81
10. Systematic review issues.	82
A. OPPT provides neither explanation nor empirical support for its revisions to the systematic review data quality criteria for epidemiological studies, which make it impossible for epidemiological studies to be scored overall as high quality.	82
B. OPPT’s approach taken to evidence integration in the draft methylene chloride risk evaluation does not align with best practices as reflected and shared by leading systematic review methods for chemical assessment (e.g., OHAT, NavGuide, IRIS).	82
C. EPA’s evaluation of study quality is insufficient and inconsistent.	83

1. Broad/cross-cutting concerns

A. EPA has given insufficient consideration to vulnerable subpopulations.

EPA has failed to sufficiently identify and address potential hazards, exposures, and risks to several vulnerable subpopulations. Our concerns are detailed in the following sections of these comments:

- Workers and ONUs: Sections 1.B., 2.D., 5.A., 5.B., 5.C., 5.E., 8.A., 9.A.
- Consumers: Section 5.C.

- Pregnant women, infants and children: Sections 4.A., 8.C.
- Genetically susceptible subpopulations: Section 4.C.i.
- People in proximity to conditions of use or sources of contamination: Section 2.C.

B. EPA has overrelied on personal protective equipment and the adequacy of OSHA requirements.

EPA's risk determinations heavily rely on assumptions that workers, at many or most points in the value chain and lifecycle of methylene chloride, will use personal protective equipment (PPE) (gloves and respirators) and that it will be universally effective. Sections 5.A. and 5.B. of these comments provides an in-depth analysis EDF conducted of the extent and impact of this over-reliance on PPE. But EPA notes the enormous effect of these assumptions on its risk characterizations in the Executive Summary of the draft risk evaluation:

With use of *expected* PPE during relevant conditions of use, worker exposures were estimated to be reduced. This resulted in fewer conditions of use with estimated acute, chronic non-cancer, or cancer inhalation or dermal risks. With *expected* use of respiratory protection, cancer risks from chronic inhalation exposures were not indicated for most conditions of use. Similarly, with *expected* dermal protection, acute, chronic non-cancer, and cancer risks were not indicated for most conditions of use. (p. 30, emphases added)

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). In EPA's risk determination section, the agency states:

EPA determined that occupational dermal exposures were expected. For acute and chronic cancer dermal exposures, risk estimates for these pathways do not indicate risk when expected PPE was considered (gloves PF = 10 or PF = 20). For chronic non-cancer dermal exposures, while some risks are indicated with gloves PF = 10, EPA has determined that these risks are not unreasonable. (p. 428)

(See section 9.A.iv. for EDF's comments on the inadequacy of EPA's justification for the latter statement in this excerpt.)

EPA's assumptions about PPE use are wholly unsupported and unwarranted. EPA has provided no data or analysis whatsoever to support these sweeping assumptions. Rather, the agency makes clear that it does not have any actual data on respirators or gloves, such as types used and frequency, by stating elsewhere in the draft risk evaluation that:

- “[N]o data were found about the overall prevalence of the use of respirators to reduce DCM exposures and it was not possible to estimate the numbers of workers who have reduced exposures due to the use of respirators.” (p. 690)
- “Regarding glove use, 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.” (p. 110)

Instead, EPA assumed without evidence various levels of protection from different purely hypothetical PPE scenarios. EPA then found risk only where either: a) the most stringent PPE it could assume was insufficient to mitigate the risk, or b) EPA could not possibly justify any assumption that PPE would be used.

For workers (which are one example of PESS), an unreasonable risk may be indicated when risks are not adequately addressed through expected use of workplace practices and exposure controls, including engineering controls or use of personal protective equipment (PPE). (p. 424)

There is considerable evidence of major real world limitations of PPE, with regards to both the extent of use and effectiveness. In fact, OSHA has highlighted the major limitations of reliance on PPE, as has EPA in the recent past. For example, in 2016 OSHA informed EPA that respirators are the “least satisfactory approach to exposure control,” providing the following explanation:

...to be effective, respirators must be individually selected, fitted and periodically refitted, conscientiously and properly worn, regularly maintained, and replaced as necessary. The absence of any one of these conditions can reduce or eliminate the protection the respirator provides.

Respirator effectiveness ultimately relies on the practices of individual workers who must wear them. ... Furthermore, respirators can impose substantial physiological burdens on workers, including the burden imposed by the weight of the respirator; increased breathing resistance during operation; limitations on auditory, visual, and olfactory sensations; and isolation from the workplace environment.²

² Comment Letter from David Michaels, PhD, MPH, Assistant Secretary, U.S. Dep’t of Labor, Occupational Safety & Health Admin., to James J. Jones, Assistant Administrator, U.S. EPA, Office of Chem. Safety & Pollution Prevention (Oct. 25, 2016), <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2014-0650-0041>

EPA affirmed its agreement with OSHA's conclusion in its proposed TSCA section 6 rule to ban methylene chloride-based paint strippers in both consumer and commercial settings.³

It is also important to recognize that reliance on PPE as a primary measure to protect workers is counter to OSHA's Industrial Hygiene Hierarchy of Controls (HOC), a long-standing principle that prioritizes measures to eliminate or reduce the presence of a hazard in occupational settings (e.g., substitution/use of less toxic chemicals and institution of engineering controls) over measures that shift burdens onto the workers themselves, such as through reliance on PPE and warning labels. The HOC exemplifies the best available science for creating safe, healthful workplace environments.

EDF previously commented on the serious limitations of labeling and PPE, as well as the importance of adherence to the hierarchy of controls to limit workplace exposures.⁴ EDF incorporates and reiterates the points made in those comments here.

As discussed in detail in section 5.E., the OSHA Permissible Exposure Limit (PEL) for methylene chloride is not health-protective. It was last updated over 20 years ago, and, in the context of paint and coating removal exposures, OSHA itself has indicated that the PEL would be insufficient to protect workers from the risks.⁵

Furthermore, OSHA's database of inspections demonstrates significant noncompliance with OSHA respiratory protection requirements such as those that apply to methylene chloride. In fiscal year 2018 alone, OSHA cited 2,892 violations of the respiratory protection standard identified in 1,281 separate inspections.⁶ Violations of the respiratory standard were the 4th most

³ Methylene Chloride and N-Methylpyrrolidone; Regulation of Certain Uses Under TSCA Section 6(a), 82 Fed. Reg. 7464, 7481 (proposed Jan. 19, 2017), <https://www.regulations.gov/docket?D=EPA-HQ-OPPT-2016-0231>.

⁴ See, e.g., EDF Comments on TSCA Review and Scoping for First 10 Chemicals under the Lautenberg Act at 6 (Mar. 15, 2017), <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0736-0046>; EDF Comments on Significant New Uses of Chemical Substances; Updates to the Hazard Communication Program and Regulatory Framework; Minor Amendments to Reporting Requirements for Premanufacture Notices (Nov. 21, 2016), <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2014-0650-0052>.

⁵ Letter from David Michaels, PhD, MPH, Assistant Secretary, U.S. Dep't of Labor, Occupational Safety & Health Admin., to James J. Jones, Assistant Administrator, U.S. EPA, Office of Chem. Safety & Pollution Prevention (Mar. 31, 2016), <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0231-0153>.

⁶ U.S. Department of Labor, Occupational Safety and Health Administration, Industry Profile for OSHA Standard 19100134, https://www.osha.gov/pls/imis/industryprofile.stand?p_esize=&p_stand=19100134&p_state=FEFederal&p_type=5 (last visited Sept. 9, 2019). These FY 2018 statistics have been replaced with the FY 2019 data and appear not to be currently accessible anymore.

common type of violation in OSHA inspections that year, exceeded only by those for two categories of physical hazard and the Hazard Communication Standard.⁷

Even when respirators and gloves *are* used, workers may still be exposed to methylene chloride. Organic solvents like methylene chloride 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. Elsewhere, EPA has acknowledged ensuring protection necessitates use of air-supplied respirators for methylene chloride.⁸ This onerous need led EPA to decide it would not be realistic to assume that workers wear respirators under many of methylene chloride's conditions of use. But other than this acknowledgment of the limitations of respirators, EPA still assumed that for many other conditions, supplied-air respirators (and not less effective types) would routinely be used and be universally effective in those settings.

Gloves may also experience chemical breakthrough (p. 110) and provide limited protection from methylene chloride exposure. EPA acknowledges that protection varies greatly with different glove materials, even recommending specific material types (pp. 594-597). Despite acknowledging this critical issue, the agency cites no data on actual use of such gloves versus less effective or ineffective alternatives, and instead simply assumes default glove protection factors (PFs) and disregards the potential for occlusion to increase exposure (see section 5.C.iv. for further discussion of EPA's failure to assess heightened exposure due to occlusion).

In a few places in the draft, EPA very briefly acknowledges some of the limitations of PPE (e.g., p. 109), and it makes a single mention of the preferability of other options higher up in the industrial hygiene hierarchy of controls (p. 595). But when it comes to determining risk, those limitations and preferences fall away and EPA exclusively relies on "expected" use of PPE to eliminate many of the risks or to understate the extent and magnitude of the risks it has identified (see sections 5.A. and 5.B. of these comments for a detailed analysis documenting the extent of EPA's reliance). As just one example, EPA finds no unreasonable risk for acute (15-minute) non-cancer effects from inhalation during processing of methylene chloride 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 assigned protection factor (APF) of 25 (see Table 4-9, p. 307).

⁷ U.S. Department of Labor, Occupational Safety and Health Administration, Top 1- Most Frequently Cited Standards, <https://www.osha.gov/top10citedstandards> (last visited Nov. 26, 2019).

⁸ Methylene Chloride and N-Methylpyrrolidone; Regulation of Certain Uses Under TSCA Section 6(a), 82 Fed. Reg. 7464, 7474 (proposed Jan. 19, 2017), <https://www.regulations.gov/docket?D=EPA-HQ-OPPT-2016-0231>.

EPA's reliance on PPE is not merely a policy determination. It is a huge assumption that dramatically alters EPA's risk characterizations for methylene chloride. EPA's reliance on PPE is also the foundation of a large fraction of EPA's risk determinations for workers even though EPA has acknowledged it has no actual data on the extent or effectiveness of PPE use, as discussed earlier. EPA's reliance on PPE leads the agency to understate the extent and magnitude of the risk where it does identify unreasonable risk. *See* sections 5.A. and 5.B. of these comments. EPA's failure to provide *any* supporting data that PPE is universally used and effective, as assumed in its risk determinations for many conditions of use (COUs), is a glaring flaw in this draft risk evaluation.

In its risk determinations, EPA has masked the extent of its reliance on PPE, by failing to be clear about when PPE (as well as engineering controls) are and are not assumed. This point was repeatedly made by SACC members during its September 10-12, 2019, peer review meeting on 1-BP.

Section 5.A. of these comments presents an analysis showing that, for virtually every condition of use of methylene chloride where respiratory PPE might plausibly be used, in most of those cases EPA found no unreasonable risk only by assuming that workers wear respiratory PPE to protect against inhalation exposures. For those conditions of use where EPA did identify unreasonable risk, it was compelled to do so because even the most stringent level of respiratory PPE protection EPA examined and assumed would be used was insufficient to eliminate that risk.

Section 5.B. of these comments presents an analysis showing that, 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. For seven of these scenarios, EPA dismissed excessive chronic non-cancer risks it identified, even after assuming glove use, because the risk estimates were "very nearly at the benchmarks."

C. EPA's draft risk evaluation suffers from a lack of transparency.

i. EPA must obtain and make public the full studies on which it relies.

It is not clear whether EPA has access to full studies on which it relies in the risk evaluation. In prior draft risk evaluations, as EDF has noted in its comments,⁹ EPA has relied on only industry-prepared study summaries. EPA not only needs to obtain copies of the full studies, it also needs

⁹ EDF Comments on the Draft Risk Evaluation of 1-Bromopropane at p. 18, <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0235-0047>; EDF Comments on the Draft Risk Evaluation of 1,4-dioxane at p. 17, <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0238-0058>.

to make full copies of studies on which it relies available to the public. As EDF has explained in prior comments, there are numerous reasons that it is important that the public have access to full studies and the underlying information, not simply robust or other study summaries.¹⁰ Without access to full studies, EPA and the public will be challenged or unable to assess and comment on the quality of the studies used by the agency, including the extent to which the requirements of section 26(h) and 26(i) are met.

Even the best study summaries are incomplete descriptions that do not allow for an independent examination of study quality and conclusions reached by authors. Common examples of such conclusions include, “findings were not statistically significant,” “findings are within the range of historical controls,” and “effects observed were non-linear [and therefore biologically questionable or irrelevant].” Divorced from the details of the actual design and results of a study, it is impossible to evaluate the appropriateness of such conclusions.

EPA itself has forthrightly stated this very need. In a request EPA sent to industry requesting full studies on Pigment Violet 29, obtained through a FOIA request made by EDF and other groups,¹¹ EPA states (emphasis added):

[S]ummary study results do not provide sufficient information upon which the hazard(s) and risk(s) from manufacture, distribution in commerce, processing, use, or disposal of this substance or any combination of such activities on health or the environment can reasonably be determined or predicted. *** *EPA needs to review the full study reports to confirm the information in the summaries meets the scientific standards set forth in TSCA section 26.*

EPA should make such information public and easily searchable through online portals such as the Health and Environmental Research Online (HERO) database. EDF incorporates and reiterates the numerous points made in support of public access to full studies here. *Id.*

¹⁰ See, e.g., EDF Problem Formulation Comments at p. 61, <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0741-0085>; EDF Comments on Procedures for Chemical Risk Evaluation under the Amended Toxic Substances Control Act at p.37, <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0654-0074>; EDF Comments on the Draft Risk Evaluation of 1-Bromopropane at p. 18, <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0235-0047>.

¹¹ Letter from Maria Doa, U.S. EPA, Director of Chemical Control Division, to Martijn Schoonenberg, Sun Chemical Group p. 1 (Sept. 15, 2017) http://blogs.edf.org/health/files/2019/09/Response-1-and-6.-Letter-to-Sun-Chemical-Group-Cooperatief-U.A. PV29.9-15-17_Redacted.pdf.

ii. *EPA's risk evaluation lacks an adequate mass balance.*

As discussed by the Science Advisory Committee on Chemicals (SACC) peer-review report on EPA's 1,4-dioxane draft risk evaluation,¹² EPA's draft risk evaluations have failed to account for a chemical substance's presence and flow at the different stages of its lifecycle. In the case of methylene chloride, over 260 million pounds of methylene chloride are manufactured in or imported into the United States annually (p. 40), yet less than three million pounds of methylene chloride were identified as released to the air and less than 3,000 pounds to surface water;¹³ the draft risk evaluation does not make clear where the rest of it goes. In order to provide transparency, SACC members recommended that EPA should develop and present a mass balance for 1,4-dioxane and 1-bromopropane. EDF concurs and further recommends that the agency should do the same for methylene chloride.

While the term "mass balance" can mean different things,¹⁴ it is appropriate to look at the definition under the Emergency Planning and Community Right-to-Know Act (EPCRA), under which EPA must collect release data on chemicals through the Toxics Release Inventory (TRI). According to EPCRA, mass balance is "an accumulation of the annual quantities of chemicals transported to a facility, produced at a facility, consumed at a facility, used at a facility, accumulated at a facility, released from a facility, and transported from a facility as a waste or as a commercial product or byproduct or component of a commercial product or byproduct." 42 U.S.C. § 11023(l)(4). While EPA relies on the CDR and TRI to compile some estimates of these values, there are limitations on both of those reporting schemes that result in an incomplete picture of the chemical's lifecycle.

As reported by the National Research Council (NRC):

Congress was aware that the toxic chemical release estimates reported under [TRI] might not accurately reflect the amounts actually released from reporting facilities (U.S. Congress, House, 1986). This potential inaccuracy is based on the provision that quantities of chemical releases can be obtained from theoretical calculations, engineering estimates, or by subtracting mass balance quantities

¹² SACC July 2019 Meeting Minutes and Final Report on 1,4-dioxane and HBCD at p. 44, <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0238-0063>.

¹³ U.S. EPA, *Problem Formulation of the Risk Evaluation for Methylene Chloride* (Dichloromethane, DCM) CASRN: 75-09-2 p. 34 (May 2018), <https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/methylene-chloride-problem-formulation>.

¹⁴ National Research Council, *Tracking Toxic Substances at Industrial Facilities: Engineering Mass Balance Versus Materials Accounting* p.2 (1990), <https://www.nap.edu/read/1415/chapter/2>.

(e.g., chemical quantity purchased minus the quantity contained in the product) rather than from measurements of actual releases.”¹⁵

In order to conduct a robust and transparent risk evaluation on methylene chloride, and more generally on chemical substances, EPA must provide significantly more detail about the chemical’s lifecycle by conducting a mass balance analysis. Section 26(h)(3) requires the Administrator to consider the “degree or clarity and completeness with which [] data *** are documented,” and without a mass balance analysis EPA has not reached any reasonable degree of clarity. 15 U.S.C. § 2625(h)(3).

D. The SACC must address the scientific consequences of EPA’s “policy” determinations.

EPA has publicly stated that a number of the topics discussed at past SACC meetings on 1,4-dioxane and 1-bromopropane are in the realm of policy and are therefore not relevant to the SACC’s charge. These include:

- EPA’s decision to exclude 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;
- EPA’s decision to assume that PPE is always used and effective under many conditions of use; and
- EPA’s decision to use a benchmark cancer risk level of 1×10^{-4} to define unreasonable risk to workers.

EDF strongly disagrees that these issues are beyond the scope of the SACC. In fact, they fall squarely within the SACC’s charge. All three decisions have major direct scientific consequences, as they clearly lead to underestimations of chemicals’ risk – to the environment, the general population, workers, and vulnerable subpopulations. In the Final SACC Report for 1,4-dioxane,¹⁶ the SACC appropriately addressed some of these issues and should continue doing so in future reports with a particular emphasis on how those determinations affect the scientific accuracy and legitimacy of the risk evaluations.

Charge question 6, among others, expressly directs the SACC to address the uncertainties and assumptions underlying the draft risk evaluation. All three of EPA’s decisions described above represent assumptions that EPA has not verified or adequately explained, and that introduce major uncertainty into its risk evaluation that EPA has not analyzed. It is vital that the SACC

¹⁵ National Research Council, *Tracking Toxic Substances at Industrial Facilities: Engineering Mass Balance Versus Materials Accounting* (1990), <https://www.nap.edu/read/1415/chapter/6>.

¹⁶ See SACC Final Report/Meeting Minutes for 1,4-Dioxane, transmitted Oct. 31, 2019, <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0237-0064>.

consider and address in its report the scientific consequences of these assumptions and decisions on EPA's characterization of exposure, hazard, and risk. Each of these assumptions are addressed below.

First, the statutory-based exclusions. As described in section 2.B. of these comments, EPA has asserted that exposures to the general population are “adequately managed” without any analysis whatsoever of the standards under the other statutes, including standards that are not strictly health based, unlike TSCA's standard. EPA devoted less than four pages to justify its decision to eliminate entire pathways, and provided no data or analysis of the exposures and risks that remain and their contribution to total exposure and risk.¹⁷

EPA has failed to provide any scientific rationale for this assumption, and the SACC has been charged with commenting precisely on the adequacy of the support EPA has provided for just such assumptions.

Second, as discussed in further detail in section 1.B of these comments, EPA frequently assumes PPE is used and effective in order to find no unreasonable risk to workers, even though EPA has stated elsewhere in the draft risk evaluation that it does not have data on use of respirators and gloves.

In order for the SACC to fully evaluate this assumption, the SACC should request that EPA provide any feedback EPA 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.

Third, EPA's unprecedented use of 1 in 10,000 as the cancer risk benchmark for workers also clearly underestimates risk, and flies in the face of EPA's longstanding policy “that it should reduce risks to less than 1×10^{-6} for as many exposed people as reasonably possible.” National Emission Standards for Hazardous Air Pollutants; Radionuclides, 54 Fed. Reg. 51,654, 51,686 (Dec. 15, 1989). Workers are specifically identified under TSCA as a vulnerable subpopulation warranting special protection. See section 9.A.ii. for more detail on this issue.

In sum: TSCA specifically states that the purpose of the SACC is to provide advice on “scientific and technical aspects” related to implementation of TSCA, and EPA's sweeping assumptions regarding exposures from environmental releases, PPE use, and adequacy of reliance on a less protective cancer risk benchmark for workers have direct impacts on the scientific integrity of EPA's implementation of TSCA.

¹⁷ Those four pages were in the problem formulation for methylene chloride, and the draft risk evaluation merely alluded to that explanation with no additional analysis. See Methylene Chloride Problem Formulation at pp. 54-57 and the draft risk evaluation at p. 33.

The SACC needs to address the scientific consequences of each of these decisions. At the very least, it is the SACC's responsibility to state clearly in its report that these assumptions result in serious underestimations of risk

2. EPA has inappropriately or illegally excluded conditions of use and exposures.

A. EPA failed to analyze certain reasonably foreseen conditions of use.

In the problem formulation, EPA identified certain conditions of use for methylene chloride that EPA also excluded from consideration in its draft risk evaluation. (p. 166). According to the draft risk evaluation, the “[p]roblem formulation also included mention of consumer uses such as metal products not covered elsewhere, apparel and footwear care products and laundry and dishwashing products. Those conditions of use are not evaluated here as no applicable consumer products were found for these uses after additional review.” (p. 42). Oddly, EPA still considered these uses for “Industrial and Commercial Uses,” and indeed, EPA found that these conditions of use present an unreasonable risk (p. 35) (listing of “Industrial and Commercial Uses that Present an Unreasonable Risk”: “[f]or metal products not covered elsewhere for non-aerosol degreases,” “[a]s an apparel and footwear care product for post market waxes and polishes,” and “[a]s a laundry and dishwashing product”). Therefore, it appears that EPA excluded these conditions of use from its analysis of consumer uses; EPA still included these conditions of use as industrial and commercial uses. EPA should clarify its treatment of these conditions of use. In addition, EPA should analyze the consumer uses in these circumstances because methylene chloride's use in the industrial and commercial context makes its at least reasonably foreseen that methylene chloride is or could be used in the same manner in the consumer context.

While compelling evidence of the absence of consumer products could establish that these circumstances are not “known” conditions of use, EPA has not addressed whether these circumstances are “reasonably foreseen” conditions of use. *See* 15 U.S.C. § 2602(4) (“The term ‘conditions of use’ means the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or *reasonably foreseen* to be manufactured, processed, distributed in commerce, used, or disposed of.”) (emphasis added). Methylene chloride is used for these specific purposes in the industrial and commercial context, and therefore it is at least reasonably foreseen that it is or could be used in the same manner in consumer products.

Congress included “reasonably foreseen” circumstances within TSCA with the express goal of ensuring that EPA swept more broadly than known (or intended) uses; EPA cannot evade that duty by limiting its analysis to conditions of use with evidence of current, ongoing use—such an interpretation would effectively limit EPA's analysis to “known” uses. While there may well be circumstances in which a use that is not currently occurring could be said to be not “reasonably

foreseen” at this time, the term surely cannot be read in such a way that only uses that are known to be current are “reasonably foreseen” as that would read it out of existence and collapse the inquiry to one where a use must be “known” to be considered “reasonably foreseen.”

Reasonably foreseen is a term of art with a long history in the law; it is well established under the law that “[a] natural and probable consequence is a foreseeable consequence. But to be reasonably foreseeable [t]he consequence need not have been a strong probability; a possible consequence which might reasonably have been contemplated is enough.” *People v. Medina*, 209 P.3d 105, 110 (Cal. 2009) (internal citations and quotation marks omitted). When a chemical is used in a commercial setting and where “there is no evidence to show that the manufacturer, wholesaler, or retailer of a hazardous substance sought to limit sales of the product to industrial or professional users, it is reasonably foreseeable that household consumers will have access to the product.” *Canty v. Ever-Last Supply Co.*, 296 N.J. Super. 68, 78-79 (N.J. Super. Ct. 1996). Even where a product is “labeled for industrial use,” it may be reasonably foreseeable that the product may ultimately be used by a consumer. *See No. 98-1979 v. Sunnyside Corp.*, 2000 Wisc. App. LEXIS 118, *12 (Ct. of Appeals WI, Feb. 15, 2000). Here, given methylene chloride’s industrial and commercial uses, the potential for these uses to be expanded to consumer use is reasonably foreseeable.

B. EPA has inappropriately excluded exposures based on other statutes.

Referencing its earlier problem formulation, EPA has excluded from its risk evaluation all general population exposures to methylene chloride, based on EPA’s assertion – unsupported by any actual data or analysis – “that chemicals present in various media pathways (i.e., air, water, land) fall under the jurisdiction of existing regulatory programs and associated analytical processes carried out under other EPA-administered statutes and have been assessed and effectively managed under those programs.” (p. 428; see also pp. 33, 37).

Aside from the absent legal basis, these exclusions present significant health concerns. For example, in the problem formulation for methylene chloride (pp. 43-44), EPA explicitly relies on the Clean Air Act (CAA) to dismiss the need to assess exposures to methylene chloride from air emissions. Methylene chloride is regulated as a hazardous air pollutant (HAP) under the CAA, but the standards under the CAA for HAPs are set for individual source categories, meaning that the exposures to methylene chloride from all sources in combination are never considered. In a recent proposed rule under the CAA for a source category that includes methylene chloride emissions, EPA has stated that:

Although we are interested in placing source category and facility-wide HAP risk in the context of total HAP risk from all sources combined in the vicinity of each source, we are concerned about the uncertainties of doing so. Estimates of total HAP risk from emission sources other than those that we have studied in depth

during this RTR review would have significantly greater associated uncertainties than the source category or facility-wide estimates. Such aggregate or cumulative assessments would compound those uncertainties, making the assessments too unreliable.

National Emission Standards for Hazardous Air Pollutants: Rubber Tire Manufacturing Residual Risk and Technology Review, 84 Fed. Reg. 58,268, 58,273 (proposed Oct. 30, 2019). This explanation of EPA's approach to assessments under the CAA makes clear that EPA does not look at overall risk from a chemical substance. Therefore, EPA's approach to its draft risk evaluations under TSCA ensures that EPA *never* evaluates, and the public never finds out, the risk from all air emissions of methylene chloride or any other chemical substance. The SACC has previously noted the flaws in this approach to EPA.¹⁸

In addition, even by its own account, EPA's CAA regulations do not eliminate risk to exposed populations. For example, when EPA promulgated a regulation "to limit emissions of methylene chloride (MC), trichloroethylene (TCE) and perchloroethylene (PCE) from facilities engaged in halogenated solvent cleaning," EPA did not eliminate cancer risks. National Air Emission Standards for Hazardous Air Pollutants: Halogenated Solvent Cleaning, 85 Fed. Reg. 25,138 (May 3, 2007). Instead, EPA adopted standards that it acknowledged would leave the maximum individual risk of cancer at "between 20 and 50-in-a-million and the total number of people with risks greater than 1-in-a-million would *** be *** between 500,000 and 1,000,000." *Id.* at 25,148. Thus, by EPA's own account, its CAA regulation of methylene chloride did not eliminate all risk from just these facilities, much less consider how exposure to methylene chloride from the regulated facilities might combine with exposures from other facilities and sources to increase overall risk.

EPA has also failed to acknowledge that the requirements to address human and environmental health risks it relies on derive from statutes that establish criteria different than those under TSCA.¹⁹ Many of these other statutes, for example, require EPA or other agencies to consider factors such as cost and feasibility when setting standards -- factors that TSCA explicitly forbids EPA from taking into account when assessing risks. TSCA section 6(b)(4)(A) states (emphasis added):

The Administrator shall conduct risk evaluations pursuant to this paragraph to determine whether a chemical substance presents an unreasonable risk of injury to

¹⁸ SACC July 2019 Meeting Minutes and Final Report Docket p. 18 (Oct. 31, 2019), <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0238-0063>.

¹⁹ EDF has addressed these limitations in greater detail in prior comments. *See, e.g.*, EDF Comment on the 1,4-dioxane Draft Risk Evaluation pp. 113-31, <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0238-0058>.

health or the environment, *without consideration of costs or other nonrisk factors*, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator, under the conditions of use.

The releases and exposures EPA is ignoring are far from trivial. Based on the most recent data from EPA's Toxics Release Inventory (TRI) and National Emissions Inventory (NEI), despite existing regulations under other laws, facilities release nearly 4,300,000 pounds annually of methylene chloride to air, water and land. EPA's approach effectively reduces this quantity to zero.

C. EPA needs to analyze those potentially exposed or susceptible subpopulations that face greater exposure due to their proximity to conditions of use.

TSCA § 3(12) states that “the term ‘potentially exposed or susceptible subpopulation’ means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly.” 15 U.S.C. § 2602(12). In its draft risk evaluation, EPA erroneously limits its analysis to only half of this definition; EPA discusses whether persons might face greater susceptibility to methylene chloride, but, outside of its consideration of worker and consumer exposures, EPA does not consider whether subpopulations may face a greater risk due to greater exposure. EPA must consider and analyze each of these types of subpopulations.

EPA must identify those who face greater exposures due to their proximity to conditions of use as a “potentially exposed or susceptible subpopulation” since they are a “group of individuals within the general population identified by the Administrator who, due to *** greater exposure, *may* be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture.” 15 U.S.C. § 2602(12) (emphasis added). Notably, in the problem formulations, EPA seemed to acknowledge that it should analyze these vulnerable subpopulations. *See, e.g.*, Problem Formulation for Methylene Chloride at p. 40 (“Other groups of individuals within the general population who may experience greater exposures due to their proximity to conditions of use identified in Section 2.2 that result in releases to the environment and subsequent exposures (e.g., individuals who live or work near manufacturing, processing, use or disposal sites).”).

But in the draft risk evaluation, EPA does not identify these populations as potentially exposed or susceptible subpopulations (pp. 385-87). 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's failure to consider this relevant aspect of the problem is arbitrary and capricious.²⁰

In order to accurately assess the exposure of these subpopulations, EPA should analyze the environmental pathways that lead to the exposure of these subpopulation. Thus, EPA should not exclude those pathways for the reasons given above, and in addition, EPA cannot rationally evaluate the greater exposure these subpopulations face without analyzing these pathways. EPA has provided no rationale explaining how it plans to accurately evaluate the risks faced by these subpopulations while ignoring these pathways of exposure. Instead, EPA simply fails to mention these subpopulations entirely, but ignoring these subpopulations violates EPA's duty to consider potentially exposed or susceptible subpopulations.

As part of this analysis, EPA should 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.²¹ To be clear, 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.

D. EPA excluded a number of workplace-related exposure scenarios.

EPA excluded a number of reasonably foreseen conditions of use in the workplace that should have been evaluated. During the SACC meeting to peer-review the 1,4-dioxane draft risk evaluation, concerns were raised about a number of exposure scenarios that the agency failed to consider, each of which equally applies to methylene chloride. Among those discussed are:

- Exposures from spills in the workplace, especially considering the potential for inhalation exposure from evaporation;
- "Take-home exposures," whereby the family of a worker, including children, may be exposed via contact with the worker's contaminated clothing or skin;
- Exposures of maintenance staff, especially those cleaning up spills and leaks; and
- Exposures of workers at small or medium facilities where assumptions of routine PPE use or other protections are even less likely to be valid.

With regards to the last point, as documented in section 5.A. of these comments, while we recognize that EPA did not assume use of respirators by workers under 35 conditions of use

²⁰ Notably, EPA did attempt to identify Superfund sites that may have been the source of methylene chloride detected in water monitoring data. (p. 96). However, the purpose was *not* to identify subpopulations at risk of greater exposure, but rather an attempt to identify data that it could "remove" from the draft risk evaluation. In the future, EPA should conduct these analyses to identify subpopulations at risk of greater exposure.

²¹ See Appendix A for a list of active Superfund sites containing methylene chloride.

(COUs), EPA still assumed universal use and effectiveness of respirators in the other 29 COUs. SACC members peer-reviewing 1,4-dioxane expressed concern that even if one assumes that PPE is typically used in larger, industrial facilities, smaller facilities are much less likely to require routine and effective use of protective equipment or to employ engineering controls, like closed systems. 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.

“Conditions of use” are broadly defined under TSCA to mean “the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or *reasonably foreseen* to be manufactured, processed, distributed in commerce, used, or disposed of.” 15 U.S.C. § 2602(4) (emphasis added). Each of the circumstances described above—spills, take home exposures, exposures to maintenance staff, and exposures without appropriate PPE—is a “reasonably foreseen” aspect of the circumstances under which methylene chloride is manufactured, processed, distributed, used, or disposed of. It is well established under the law that “[a] natural and probable consequence is a foreseeable consequence. But to be reasonably foreseeable [t]he consequence need not have been a strong probability; a possible consequence which might reasonably have been contemplated is enough.” *People v. Medina*, 46 Cal. 4th 913, 920 (Cal. 2009) (internal citations and quotation marks omitted).

“Reasonably foreseen” is a term of art with a long history in the law, and EPA should turn to the ample precedent interpreting this language to inform implementation of this legal requirement. Spills and leaks are undoubtedly reasonably foreseeable, and indeed, when preparing environmental impact statements (EISs) for federal projects, the federal government regularly analyzes the potential for spills and leaks because they are reasonably foreseen aspects of such projects. *See, e.g., Sierra Club v. Clinton*, 689 F. Supp. 2d 1123, 1139 (D. Minn. 2010) (describing analysis of potential for leaks and spills).

And in the tort context, courts have found that spills and leaks can be reasonably foreseen. *See, e.g., Monroe v. Safeway, Inc.*, 2004 Wash. App. LEXIS 672, *6 (Ct. Appeals Wash. 2004); *Ceasar v. Wal-Mart Stores, Inc.*, 787 So. 2d 582, 588 (Ct. Appeals. La. 2001) (finding spill reasonably foreseeable); *Lumbermens Mut. Cas. Co. v. Banco Espanol De Credito*, 2006 U.S. Dist. LEXIS 75728, *25 (S.D.N.Y. Oct. 13, 2006) (describing leak as reasonably foreseeable); *Goehler v. Wal-Mart Stores, Inc.*, 2000 U.S. App. LEXIS 20932, *1-2 (4th Cir. Aug. 17, 2000) (same).

Take-home exposure, maintenance staff exposure, and exposure of persons not using PPE are equally reasonably foreseen.

3. EPA must adopt a linear, no-threshold approach for methylene chloride's carcinogenicity.

A. There is strong support for methylene chloride's cancer classification and a mutagenic mode of action.

EPA states (p. 264):

There is sufficient evidence of methylene chloride carcinogenicity from animal studies. Methylene chloride produced tumors at multiple sites, in males and females, in rats and mice, by oral and inhalation exposure, and in multiple studies.

These statements are wholly consistent with numerous other classifications:

- The International Agency for Research on Cancer (IARC) has classified methylene chloride as “probably carcinogenic to humans (Group 2A) in 2016.”²²
- The National Toxicology Program's (NTP) *Report on Carcinogens* concluded in its 14th Report on Carcinogens issued in 2016 that methylene chloride is “reasonably anticipated to be a human carcinogen.”²³
- EPA's IRIS program has classified methylene chloride as “Likely to be carcinogenic to humans.”²⁴

EPA cites significant information that supports a mutagenic/genotoxic MOA for methylene chloride (pp. 245-247). EPA appropriately concludes (p. 247): “Available data do not suggest that modes of action other than genotoxicity are relevant.”

EPA reviews the extensive evidence on methylene chloride's genotoxicity in Section 3.2.3.2.1 and Appendix K of the draft risk evaluation and appropriately echoes both the 2011 IRIS assessment and the International Agency for Research on Cancer (IARC) monograph in concluding that (*emphasis added*):

... methylene chloride has a mutagenic MOA involving DNA-reactive metabolites produced via a metabolic pathway catalyzed by GSTT1. There are numerous genotoxicity tests showing positive results for methylene chloride, including

²² IARC, *Dichloromethane* in IARC MONOGRAPHS ON THE EVALUATION OF CARCINOGENIC RISKS TO HUMANS p. 243 (2016), <https://monographs.iarc.fr/wp-content/uploads/2018/06/mono110-04.pdf>.

²³ Nat'l Toxicology Program, *Report on carcinogens Monograph for dichloromethane* at p. 1, <https://ntp.niehs.nih.gov/ntp/roc/content/profiles/dichloromethane.pdf>.

²⁴ EPA IRIS website, https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=70.

assays for mutagenicity in bacteria and mutagenicity, DNA damage, and clastogenicity in mammalian tissues in vitro and in vivo. (p. 265)

and

The weight-of-evidence analysis for [liver and lung tumors] was sufficient to conclude that DCM-include tumor development operates through a mutagenic mode of action.” (p. 698)

Information supporting these conclusions are provided in IARC’s classification (p. 243, *emphasis* in original):

A Group 2A evaluation was also supported by *sufficient* evidence in experimental animals, and the *strong* evidence that the metabolism of dichloromethane via GSTT1 leads to the formation of reactive metabolites, that GSTT1 activity is strongly associated with genotoxicity in vitro and in vivo, and that GSTT1-mediated metabolism of dichloromethane occurs in humans.²⁵

In tandem EPA has reviewed the potential alternative MOAs and appropriately concludes (p. 247): “Available data do not suggest that modes of action other than genotoxicity are relevant.”

Based on the weight of the scientific evidence, EPA states (p. 266):

In accordance with U.S. EPA (2005a) *Guidelines for Carcinogen Risk Assessment*, methylene chloride is considered “likely to be carcinogenic to humans” based on sufficient evidence in animals, limited supporting evidence in humans, and mechanistic data showing a mutagenic MOA relevant to humans. Therefore, this hazard was carried forward for dose-response analysis.

We strongly support the agency’s decision to adhere to the *EPA Guidelines for Carcinogen Risk Assessment* and use the default approach of linear non-threshold extrapolation in the cancer risk modeling for methylene chloride.

²⁵ IARC, *Dichloromethane* in IARC MONOGRAPHS ON THE EVALUATION OF CARCINOGENIC RISKS TO HUMANS p. 243 (2016), <https://monographs.iarc.fr/wp-content/uploads/2018/06/mono110-04.pdf>.

B. The scientifically sound and health-protective approach is to use linear extrapolation in cancer dose-response modeling for methylene chloride.

i. Justification based on existing guidance

The information presented above: 1) demonstrates that evidence supports the potential for a genotoxic MOA, and 2) casts doubt on the plausibility of alternative MOAs. Even were the evidence deemed insufficient to identify with certainty a genotoxic MOA, there is longstanding EPA policy guidance and precedent supporting a default to a no-threshold, linear extrapolation method for cancer dose-response modeling.

The agency's own 2005 cancer guidelines state that:

When the weight of evidence evaluation of all available data are insufficient to establish the mode of action for a tumor site and when scientifically plausible based on the available data, linear extrapolation is used as a default approach, because linear extrapolation generally is considered to be a health-protective approach.²⁶

EPA must follow its guidance documents in preparing the final risk evaluation. “An agency may not ... depart from a prior policy *sub silentio* or simply disregard rules that are still on the books.” *FCC v. Fox TV Stations, Inc.*, 556 U.S. 502, 515 (2009). EPA's guidance documents reflect the considered judgment of the agency on major factual issues, and an agency may not lightly adopt new policies reflecting contradictory factual findings without providing a detailed justification for the shift in position. *Id.* Moreover, EPA's Risk Evaluation Rule provides that “EPA guidance will be used, as applicable where it represents the best available science appropriate for the particular risk evaluation.” 40 C.F.R. § 702.41(a)(2). Thus, EPA must use its guidance in this risk evaluation unless EPA can establish that the guidance does not represent the best available science appropriate for this particular risk evaluation.

ii. Justification based on human population variability and other real-world considerations to protect public health

EPA must employ health-protective approaches to dose-response modeling, as described at length in the National Research Council's report, *Science and Decisions: Advancing Risk Assessment*. In this report, the NRC committee specifically provides important perspective on

²⁶ U.S. EPA, *Guidelines for Carcinogen Risk Assessment* at pp. 3-21 (Mar. 2015), https://www.epa.gov/sites/production/files/2013-09/documents/cancer_guidelines_final_3-25-05.pdf.

the need to conduct a linear extrapolation at the population level, even where a threshold might theoretically exist. The authors state, for example, that:²⁷

- “Human variability with respect to the individual thresholds for a nongenotoxic cancer mechanism can result in linear dose-response relationships in the population.”
- “In the laboratory, nonlinear dose-response processes ... may be found to cause cancer in test animals. However, given the high prevalence of these background processes, given cancer as an end point, and given the multitude of chemical exposures and high variability in human susceptibility, the results may still be manifested as low-dose linear dose-response relationships in the human population.”

Overall, the NRC report concluded that “***cancer and noncancer responses [to chemical exposures] be assumed to be linear as a default***.”²⁸ The NRC committee called for a unified approach using linear extrapolation to account for both background exposures and the wide range of variability in individual susceptibility. It argued that this approach also improves the risk characterization and ultimately risk management decisions by providing quantification of excess population risk rather than a margin of exposure.

In their *State-of-the-science workshop report: issues and approaches in low-dose-response extrapolation for environmental health risk assessment*, White et al. (2009)²⁹ also highlight that:

At the human population level *** biological and statistical attributes tend to smooth and linearize the dose-response relationship, obscuring thresholds that might exist for individuals. Most notable of these attributes are population variability, additivity to preexisting disease or disease processes, and background exposure-induced disease processes.

The 2016 amendments to TSCA made explicit and strengthened EPA’s obligation to consider risks to and protect subpopulations that may be more exposed or more susceptible to the effects of chemical exposure than the general population. To meet this statutory requirement, EPA must use a linear non-threshold modeling approach.

In summary, 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,”

²⁷ NAT’L RESEARCH COUNCIL, SCIENCE AND DECISIONS: ADVANCING RISK ASSESSMENT at chp. 5, pp. 130-131 (2009), <https://www.ncbi.nlm.nih.gov/pubmed/25009905>.

²⁸ *Id.* at chp. 5, p. 180.

²⁹ Ronald H. White, et al., *State-of-the-science workshop report: issues and approaches in low-dose-response extrapolation for environmental health risk assessment*, 117:2 ENVTL. HEALTH PERSPECTIVES 283-87 (2008), <https://www.ncbi.nlm.nih.gov/pubmed/19270800> (emphasis added).

and 4) the clear presence of individuals with preexisting health conditions, metabolic or genetic variability, or other factors that make them more susceptible to methylene chloride 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).

4. EPA's human health hazard assessment raises significant questions and concerns.

A. EPA fails to acknowledge that methylene chloride has the potential to transfer through the placenta to a developing fetus.

In the discussion of Toxicokinetics (Section 3.2.2), EPA has neglected to acknowledge the potential for placental transfer of methylene chloride. The 2011 IRIS assessment stated:

Dichloromethane is capable of crossing the placental barrier and entering the fetal circulation. Anders and Sunram (1982) reported that when pregnant Sprague Dawley rats (n = 3) were exposed to 500 ppm dichloromethane for 1 hour on gestational day (GD) 21, mean maternal blood levels were 176 nmol/mL (SEM 50), while fetal levels were 115 nmol/mL (SEM 40). The levels of CO [carbon monoxide],³⁰ a metabolite of dichloromethane, were similar in both the maternal blood (167 nmol/mL, SEM 12) and fetal blood (160 nmol/mL, SEM 31). Withey and Karpinski (1985) also reported higher maternal compared with fetal dichloromethane levels based on a study of five pregnant Sprague-Dawley rats exposed to 107–2,961 ppm of dichloromethane. Maternal blood levels of dichloromethane were 2–2.5-fold higher than those found in the fetal circulation.³¹

TSCA requires that EPA consider exposure to potentially exposed or susceptible subpopulations. As such, EPA must include reasonably available information on placental transfer and sufficiently account for such potential exposure to the fetus. In its draft risk evaluation, EPA acknowledges that fetuses can be more susceptible to effects induced by exposure to methylene chloride: "Hemoglobin in the fetus has a higher affinity for CO than does adult hemoglobin. Thus, the 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 (OEHHA, 2008b)" (p. 32).

³⁰ As noted in the IRIS assessment, methylene chloride is metabolized to CO through a cytochrome P450 pathway that predominates at low exposure levels.

³¹ U.S. EPA, *Toxicological Review of Dichloromethane (Methylene Chloride)* p. 9 (2011), https://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/0070tr.pdf.

B. EPA has failed to include any estimate of acute cancer risks.

Despite EPA's acknowledgment that the weight of the scientific evidence indicates methylene chloride is a mutagenic carcinogen and that linear extrapolation is warranted (p. 29), the agency has chosen not to estimate cancer risks based on acute exposures for DCM. As an explanation, EPA states only that the [r]elationship is not known between a single short-term exposure to DCM and the induction of cancer in humans" (p. 699).

However, the National Research Council (NRC) states:³²

Guidance on the development of short-term exposure levels, published by the NRC, identified cancer as one of the potential adverse health effects that might be associated with short-term inhalation exposures to certain chemical substances (NRC 1993a). That guidance document discusses and recommends specific risk-assessment methods for known genotoxic carcinogens and for carcinogens whose mechanisms are not well understood. As a first approximation, *the default approach involves linear low-dose extrapolation from an upper confidence limit on theoretical excess risk*. Further, the NRC guidance states that *the determination of short-term exposure levels will require the translation of risks estimated from continuous long-term exposures to risks associated with short-term exposures*. Conceptually, the approach recommended for genotoxic carcinogens adopted the method developed by Crump and Howe (1984) for applying the linearized multistage model to assessing carcinogenic risks based on exposures of short duration.

Later in the same document (p. 118), the NRC summarizes: "Guidance published by the NRC (1993a) states that the setting of AEGLs (CEELs) [acute exposure guideline levels (for what are termed "community emergency exposure levels")] should involve linear low-dose extrapolation from an upper confidence limit on excess risk for genotoxic carcinogens."

As stated in this NRC report, the decision to conduct such extrapolation and modeling should be based on the "sound biological and statistical principles." EDF is concerned 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. In particular, given that 1) the agency recognizes that "the weight-of-evidence analysis...was sufficient to conclude that DCM-induced tumor development operates through a mutagenic mode of action (U.S. EPA, 2011)" (p. 698) and 2) a mutagenic MOA suggests a role for "a single direct reaction, specifically, a single hit in a single

³² Nat'l Research Council, *Standard operating procedures for developing acute exposure guideline levels for hazardous chemicals*, pp. 111-112 (2001), <https://www.epa.gov/aegl/standing-operating-procedures-developing-acute-exposure-guideline-levels-aegls-hazardous> (emphasis added).

target (Kirsch-Volders et al., 2000),”³³ a linear low-dose extrapolation from chronic to acute exposures would be the appropriate approach to take for methylene chloride.

It is possible, though, that even a linear extrapolation from chronic cancer bioassays may underestimate the cancer risk of short-term exposures. Halmes et al., 2000 lends support to the potential for short-term exposures to result in similar or higher cancer risks than even chronic lifetime exposures.³⁴ The study used NTP data where both shorter term and full lifetime studies had been conducted.

EPA’s current approach assumes acute exposures to methylene chloride, including to consumers, pose *zero* cancer risk – an assumption that is clearly not warranted based on the weight of the evidence. EPA needs to apply an extrapolation that provides a scientifically sound estimate for cancer risk from acute and short-term exposures to methylene chloride. As EDF stated in our comments on EPA’s problem formulations (p. 81):

EPA must closely examine any effect it believes to arise only from chronic exposures to determine whether in fact this is true across the diverse human population, including where potentially exposed or susceptible subpopulations may be at increased risk for effects after shorter periods of exposure compared to the general population.

C. EPA’s calculations of inhalation unit risk (IUR) for cancer are flawed and lack transparency.

i. EPA’s IUR calculation gives insufficient consideration to susceptible subpopulations.

Susceptibility to the carcinogenic effects of methylene chloride varies in the human population due to polymorphisms in a type of glutathione S-transferase gene (GST-T1).³⁵ Individuals with the homozygous positive genotype (GST-T1 +/+) can metabolize methylene chloride via the GST pathway, which is associated with formation of reactive DNA adducts and subsequent increases in cancer risk. Compared to GST-T1 +/+ individuals, those with the heterozygous positive genotype (GST-T1 +/-) have lower rates of GST metabolism and therefore a relatively lower cancer risk associated with methylene chloride exposure. In contrast, individuals with the homozygous negative genotype (GST-T1 -/-) are unable to metabolize via the GST pathway and are thus not considered to be at risk for the carcinogenic effects of methylene chloride. Haber et

³³ Zoë Gillespi, et al., *Risk assessment approaches for carcinogenic food contaminants*, 1:1 INT’L FOOD RISK ANALYSIS J. 1-18 (2011), <https://hrcak.srce.hr/file/107066>.

³⁴ N. Christine Halmes, et al., *Reevaluating cancer risk estimates for short-term exposure scenarios*, 58:1 TOXICOLOGICAL SCIENCES 32-42 (2000), <https://academic.oup.com/toxsci/article/58/1/32/1658920/#24341943>.

³⁵ U.S. EPA, *Toxicological Review of Dichloromethane (Methylene Chloride)* (2011), https://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/0070tr.pdf.

al. (2002) estimated the prevalence of the GST-T1 +/+, GST-T1 +/- and GST-T1 -/- genotypes in the U.S. population to be approximately 32%, 48% and 20%.³⁶

In calculating the IUR in the draft risk evaluation, EPA sampled from the “full distribution of GSTT genotypes in the human population ((GSTT1+/+ , GSTT1+/- and GSTT1 -/-)” (p. 659). However, this approach was rejected by EPA in its 2011 IRIS assessment, which stated:

The inclusion of the GST-T1 null subpopulation in effect dilutes the risk that would be experienced by those who carry a GST-T1 allele by averaging in nonresponders (i.e., the GST-T1-/- genotype). Thus, the cancer oral slope factor was derived specifically for carriers of the GST-T1 homozygous positive (+/+) genotype, the population that would be expected to be most sensitive to the carcinogenic effects of dichloromethane given the GST-related dose metric under consideration.³⁷

Thus, EPA’s decision in the draft risk evaluation to sample from the full distribution of genotypes across the population dilutes the risk to sensitive GSTT1 +/+ subpopulations. EPA claims that “[u]se of the upper-bound estimate for the full population distribution of the GSTT1 genotypes is considered sufficiently protective of sensitive subpopulations” (p. 659), but this is simply inaccurate – as explained by the excerpt from the IRIS assessment quoted above. EPA should instead calculate the IUR based on sampling from a distribution of GSTT1 +/+ sensitive subpopulations to ensure sufficient protection for these individuals.

ii. *EPA’s IUR calculations lack transparency.*

a. *Modeling based on Aiso et al. 2014*

EPA presents modeling based on Aiso et al. 2014,³⁸ which was not available at the time of prior evaluations of methylene chloride, which relied on NTP 1986.³⁹ According to the authors of Aiso et al.:

³⁶ Lynne Haber, et al., *Genetic polymorphisms in assessing interindividual variability in delivered dose*, 35:2 REGULATORY TOXICOLOGY & PHARMACOLOGY 177-79 (Apr. 2002), <https://www.ncbi.nlm.nih.gov/pubmed/12052003>.

³⁷ U.S. EPA, *Toxicological Review of Dichloromethane (Methylene Chloride)* p. 220 (2011), https://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/0070tr.pdf.

³⁸ Shigetoshi Aiso, et al., *Inhalation carcinogenicity of dichloromethane in rats and mice*, 26:8 INHALATION TOXICOLOGY 435-451 (June 2014), <https://www.ncbi.nlm.nih.gov/pubmed/24909451>.

³⁹ Nat’l Toxicology Program, *Toxicology and Carcinogenesis Studies of Dichloromethane (Methylene Chloride) (CAS No. 75-09-2) In F344/N Rats and B6c3ft Mice (Inhalation Studies)* (1986),

The major difference in the two studies is that while the NTP study exposed mice to two concentration of DCM, 2000 and 4000 ppm, we exposed mice to three concentration of DCM, 1000, 2000, and 4000 ppm, and we found clear evidence that exposure to 1000 ppm was carcinogenic for both male and female B6C3F1 mice as shown by an increase in bronchiolar–alveolar carcinomas in male mice exposed to 1000 ppm and higher levels of DCM and by an increase in hepatocellular adenomas in female mice exposed to 1000 ppm and higher levels of DCM.⁴⁰

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. study. Similarly, EPA suggests that the NTP study provides the “most sensitive of the best-fitting models for the malignant tumors” (p. 279). It is unclear how these results would be obtained, given the lower point of departure (POD) based on Aiso et al. 2014. 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.

b. Deviation from Bayesian modeling approaches

In contrast to the 2011 IRIS assessment, in this draft risk evaluation EPA did not employ “Bayesian fitting procedures and Bayesian model averaging” (p. 658) for dose-response modeling and extrapolation in the IUR derivation process. Regarding these procedures, the Agency’s Benchmark Dose Technical Guidance states:

The Bayesian approach facilitates combining results from different datasets to provide a more robust estimate as well as an evaluation of the uncertainty in that estimate that would take into account the variability among studies. This type of approach may lead to improvements over the more widely used methods, which only quantify the uncertainty inherent in a single study.⁴¹

EPA must provide justification for their decision to deviate from this modeling approach.

https://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr306.pdf?utm_source=direct&utm_medium=prod&utm_campaign=ntpgolinks&utm_term=tr306.

⁴⁰ Shigetoshi Aiso, et al., *Inhalation carcinogenicity of dichloromethane in rats and mice*, 26:8 INHALATION TOXICOLOGY 435-451 (June 2014),

<https://www.ncbi.nlm.nih.gov/pubmed/24909451>.

⁴¹ U.S. EPA, *Benchmark Dose Technical Guidance* p. 11 (2012),

https://www.epa.gov/sites/production/files/2015-01/documents/benchmark_dose_guidance.pdf.

c. Selection of whole-body dose metric

In the 2011 IRIS assessment, EPA stated that “[t]he recommended inhalation unit risk value [for combined liver and lung tumors]...is based on a *tissue-specific*, GST-internal dose metric with allometric scaling.”⁴² In this draft risk evaluation, however, EPA selects the “*whole-body* GST metric” (*emphasis added*) (p. 279) in estimating the combined liver and lung tumor IUR. 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.

d. Overall differences from previously derived hazard values

In the draft risk evaluation, EPA derives an IUR of 1.38×10^{-6} per mg/m³ (equivalent to 1.38×10^{-9} per ug/m³) for liver and lung tumors. This value is lower than that derived in the 2011 IRIS assessment: IUR of 1×10^{-5} per mg/m³ (equivalent to 1×10^{-8} per ug/m³, rounded from 1.3×10^{-8} per ug/m³), for reasons that are not clear. To some extent, these differences may be due to the differential consideration EPA is now giving to GSTT subpopulations, see subsection C.i. above).

Given that the Agency used the same data to derive these differing estimates, EPA needs to provide a full and transparent comparison between the approaches that lead to the different values, and a clear rationale for different decisions that were made.

e. Classification of liver foci as “non-neoplastic”

According to a footnote in the *Methylene Chloride Benchmark Dose and PBPK Modeling Report Supplemental File*, it appears that OCSPP specified that female rate acidophilic and basophilic cell foci from Aiso et al. (2014) were to be treated as “Non-Neoplastic Foci.”⁴³ As noted in this same footnote, the authors of the Aiso et al. (2014) study instead classified these as “preneoplastic.” The Aiso et al. study classification is consistent with prior toxicologic

⁴² U.S. EPA, *Toxicological Review of Dichloromethane (Methylene Chloride)* p. 238 (2011), https://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/0070tr.pdf (*emphasis added*).

⁴³ U.S. EPA, *Risk Evaluation for Methylene Chloride Supplemental File: Methylene Chloride Benchmark Dose and PBPK Modeling Report CASRN: 75-09-2* p. 8 fn. 3 (Oct. 2019), https://www.epa.gov/sites/production/files/2019-10/documents/17_draft_supplemental_file_methylene_chloride_benchmark_dose_and_pbpk_modeling_report.pdf.

pathology literature,⁴⁴ as well as the National Toxicology Program (NTP), which states that “foci are presumptive preneoplastic lesions.”⁴⁵

The justification EPA now gives for its non-neoplastic classification is that “EPA did not observe correlations between the pre-neoplastic foci and tumors in this study” (p. 229). This rationale is not intuitive to us, given the possibility that foci and tumors could appear at different times due to their different relationship to cancer progression. Absent a more explicit and compelling scientific justification for this decision (including citation to relevant references), EPA should default to classifying these foci as preneoplastic and thus also include them in the BMDS multi-tumor model.

D. EPA’s modeling decisions for acute non-cancer central nervous system (CNS) effects lack sufficient justification.

i. Derivation of points of departure (PODs)

EPA appropriately acknowledges the uncertainty that arises from converting the point of departure (POD) from the 1.5-hour exposure period used in Putz (1979) to the different selected exposure durations used in the draft risk evaluations:

EPA used a default approach (Ten Berge et al., 1986), which is a modification of Haber’s rule, to convert the POD to other exposure durations. Other methods to convert among exposure durations have been used by other programs. For instance, the AEGL program used a PBPK model that estimated methylene chloride concentrations in the brain for different exposure durations for the percent of the population who did and did not conjugate GSTT1, which affects the level of COHb in blood. The PBPK model may be slightly more precise, but when NAC/AEGL (2008) compared values using the PBPK model to default values for shorter time frames, the values were similar. Therefore, EPA used the simpler method to convert POD values among exposure durations. (p. 379)

However, EPA’s assertion that the values derived from these differing methods are “similar” is inaccurate and fails to acknowledge that the differences are non-negligible. The differences in converted PODs across the methods ranged from the PBPK method producing a 6% lower POD than the default method for the 10-minute duration to an 18% higher POD for the 1-hour

⁴⁴ Bob Thoolen, et al., *Proliferative and Nonproliferative Lesions of the Rat and Mouse Hepatobiliary System*, 38:7 TOXICOLOGIC PATHWAY 5S-81S (Dec. 2010), <https://journals.sagepub.com/doi/10.1177/0192623310386499>.

⁴⁵ Nat’l Toxicology Program, *NTP Nonneoplastic Lesion Atlas: Liver – [Basophilic, Eosinophilic, Clear cell, Mixed] Focus*, https://ntp.niehs.nih.gov/nnl/hepatobiliary/liver/foci/liver-foci_508.pdf.

duration. If a method is known to be more precise and its results are available, there is no justification for using a default. As such, EPA should use the PBPK model that the AEGL program used.

ii. *LOAEC to NOAEC uncertainty factor*

For the acute inhalation benchmark MOEs for both occupational and consumer users, EPA utilized a composite uncertainty factor (UF) of 30. To derive this UF, EPA used a default intraspecies UF of 10 and a LOAEC to NOAEC UF of 3. The only rationale EPA provided for the latter was that the study effect was “of a small magnitude” (p. 275). This decision is problematic for two reasons.

First, EPA only considers an adjustment to this UF based on the *magnitude* of effects. However, the Risk Assessment Forum’s final report, *A Review of the Reference Dose and Reference Concentration Processes*, states that “[t]he size of the LOAEL-to-NOAEL UF may be altered, depending on the *magnitude and nature* of the response at the LOAEL.”⁴⁶ Therefore, both of these components – which address the severity and burden of the effects at both the individual (e.g., degree of change in measured parameter at the LOAEL) and population (e.g., fraction of the population affected at the LOAEL) levels – must be adequately considered when adjusting this UF value. Yet in this draft risk evaluation, EPA does not provide any discussion of the *nature* of the effects and whether this should affect the selection of the LOAEC to NOAEC UF value.

Second, the LOAEC to NOAEC UF of 3 does not seem to be based on any official agency guidance and actually deviates from prior evaluations. Both EPA’s 2014 Work Plan Chemical Assessment of methylene chloride⁴⁷ and the Office of Environmental Health Hazard Assessment (OEHHA)’s 2008 Acute Reference Exposure Level (REL) and Toxicity Summary for Methylene Chloride⁴⁸ used a LOAEC to NOAEC UF of 6, resulting in a composite UF of 60. The Agency’s decision to reduce the LOAEC to NOAEC UF is unjustified and insufficiently protective of acute inhalation risks. EPA should use a LOAEC to NOAEC UF of 6.

⁴⁶ U.S. EPA Risk Assessment Forum, *A Review of the Reference Dose and Reference Concentration Processes* p. 4-44 (Dec. 2002), <https://www.epa.gov/sites/production/files/2014-12/documents/rfd-final.pdf> (emphasis added).

⁴⁷ U.S. EPA, *TSCA Work Plan Chemical Risk Assessment Methylene Chloride: Paint Stripping Use CASRN: 75-09-2* p. 74 (2014), https://www.epa.gov/sites/production/files/2015-09/documents/dcm_opptworkplanra_final.pdf.

⁴⁸ Cal. OEHHA, *Technical Supporting Document for Noncancer RELs, Appendix D.2 Acute RELs and toxicity summaries using the previous version of the Hot Spots Risk Assessment guidelines (OEHHA 1999)* p. 189 (2008), <https://oehha.ca.gov/media/downloads/crnrr/appendixd2final.pdf>.

E. EPA’s modeling decisions for chronic non-cancer effects are not sufficiently protective of public health.

- i. EPA fails to include a necessary database deficiency uncertainty factor (UF) for chronic non-cancer liver effects.*

For the chronic inhalation benchmark MOE, EPA applied a composite UF of 10. This factor was derived based on an interspecies UF of 3 and an intraspecies UF of 3 (p. 278). However, the 2011 methylene chloride IRIS assessment utilized a composite UF of 30, which additionally included an UF of 3 to account for database deficiencies.⁴⁹ Regarding the latter UF, the IRIS assessment stated that:

In consideration of the entire database for dichloromethane, a database UF of 3 was selected. This UF accounts for limitations in the two-generation reproductive toxicity study (i.e., discontinuous exposure throughout the lifecycle) and limitations in the design of the available developmental studies (including a lack of neurodevelopmental endpoints). There is an additional potential concern for immunological effects as suggested by a single acute inhalation study, specifically immunosuppressive effects that may be relevant for infectious diseases spread through inhalation.⁵⁰

In this draft risk evaluation, EPA has not provided sufficient evidence or explanation to justify its decision not to use a database UF for chronic non-cancer effects, despite acknowledging that “there is uncertainty regarding whether CNS effects, [*sic*] may be as sensitive” and that “[l]imited data preclude using this endpoint for chronic effects” (p. 385).

A database UF is further warranted given the potential for hematologic effects (ex: increased carboxyhemoglobin (COHb) levels), described in DiVincenzo & Kaplan (1981)⁵¹ and utilized as the critical effect by OEHHA in deriving its noncancer RELs⁵² – an effect not acknowledged at all in this draft risk evaluation (see subsection ii below).

⁴⁹ U.S. EPA, *Toxicological Review of Dichloromethane (Methylene Chloride)* pp. 194-196 (2011), https://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/0070tr.pdf.

⁵⁰ *Id.* at p. 196.

⁵¹ George D. DiVincenzo & C.J. Kaplan, *Uptake, metabolism, and elimination of methylene chloride vapor by humans*, 59:1 TOXICOLOGY & APPLIED PHARMACOLOGY 13—140 (June 1981), [https://doi.org/10.1016/0041-008X\(81\)90460-9](https://doi.org/10.1016/0041-008X(81)90460-9).

⁵² Cal. OEHHA, *Technical Supporting Document for Noncancer RELs, Appendix D.3 Chronic RELs and toxicity summaries using the previous version of the Hot Spots Risk Assessment guidelines (OEHHA 1999)* (2008), <https://oehha.ca.gov/media/downloads/crnrr/appendixd3final.pdf>.

- ii. *EPA's decision to ignore human evidence of hematologic effects results in a less protective risk metric.*

This draft risk evaluation has followed the 2011 IRIS assessment in choosing to base the chronic inhalation hazard evaluation on the Nitschke et al. 1988 rat study. CalEPA based its 2008 chronic REL on a human study (DiVincenzo and Kaplan 1981)⁵³ and arrived at a more protective result than did the draft risk evaluation's approach.⁵⁴ Using the human data addresses a potential concern about other sources of CO exposure; the human participants in the DiVincenzo and Kaplan 1981 study would have been exposed to background levels of CO so the study's results would reflect background exposure.

Note: EPA did not derive a risk metric, and instead performed a MOE evaluation against a Benchmark MOE = 10. To enable a comparison to the CalEPA approach, in the table below, using the information from the draft risk evaluation EPA used, we derive a risk metric analogous to that of CalEPA:

Table A: Comparison of approaches by CalEPA (2008) and EPA Draft Risk Evaluation (2019) for effects from chronic inhalation of methylene chloride

Assessment Choices	CalEPA (2008)	EPA Draft Risk Evaluation (2019)
Key Study	DiVincenzo and Kaplan 1981 (human)	Nitschke et al. 1988 (animal)
Endpoint	COHb	Hepatocyte vacuolation
POD	14 ppm CalEPA calculated the POD with a time-weighted average from the study's LOAEC of 40 ppm.	4.8 ppm Human equivalent concentration (HEC)
UFs	UF(L) = 10 UF(A) = 1 UF(H) = 10 Total UF = 100	UF(L) = 1 UF(A) = 3 UF(H) = 3 Total UF = 10 (Benchmark MOE)
Risk metric	0.1 ppm	0.48 ppm

⁵³ George D. DiVincenzo & C.J. Kaplan, *Uptake, metabolism, and elimination of methylene chloride vapor by humans*, 59:1 TOXICOLOGY & APPLIED PHARMACOLOGY 13—140 (June 1981), [https://doi.org/10.1016/0041-008X\(81\)90460-9](https://doi.org/10.1016/0041-008X(81)90460-9).

⁵⁴ METHYLENE CHLORIDE (DICHLOROMETHANE), <https://oehha.ca.gov/chemicals/methylene-chloride-dichloromethane> (last visited Nov. 26, 2019).

F. EPA fails to include all necessary uncertainty factors in calculating the benchmark margins of exposure, resulting in inaccurate risk characterizations.

In addition to the reasons laid out in section 4.E., EPA should have included an uncertainty factor for “the uncertainty associated with extrapolation from animal data when the database is incomplete.”⁵⁵ The EPA Risk Assessment Forum notes in its 2002 report, *A Review of the Reference Dose and Reference Concentration Processes*:

The database UF is intended to account for the potential for deriving an underprotective RfD/RfC as a result of an incomplete characterization of the chemical’s toxicity. 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.⁵⁶

It is imperative that EPA include a database UF in deriving its chronic non-cancer risk estimates. We believe an UF value of 10 is warranted to account for the deficiencies in the literature (such as for neurodevelopmental effects; see section 8.C.) as well as to account for EPA’s decision to not conduct modeling on hematologic endpoints (see section 4.E.ii. above). In addition, EPA’s reliance on inhalation-to-dermal extrapolation for sub-chronic/chronic effects – necessitated by the dearth of dermal toxicity data – also introduces uncertainty that EPA has failed to account for. This is discussed further in section 8.A. below.

G. EPA should migrate to a unified approach to presenting dose-specific population risks for both cancer and noncancer endpoints.

More broadly, EPA must employ health-protective approaches to dose-response modeling, as described at length in the National Academy of Sciences (NAS) report, *Science and Decisions*:

⁵⁵ U.S. EPA Risk Assessment Forum, *A Review Of The Reference Dose And Reference Concentration Processes* p. 4-38 (Dec. 2002), <https://www.epa.gov/sites/production/files/2014-12/documents/rfd-final.pdf>; REFERENCE DOSE (RFD): DESCRIPTION AND USE IN HEALTH RISK ASSESSMENTS, <https://www.epa.gov/iris/reference-dose-rfd-description-and-use-health-risk-assessments#1.4> (last visited Jan. 14, 2019).

⁵⁶ U.S. EPA Risk Assessment Forum, *A Review Of The Reference Dose And Reference Concentration Processes* p. 4-44 (Dec. 2002), <https://www.epa.gov/sites/production/files/2014-12/documents/rfd-final.pdf>.

Advancing Risk Assessment.⁵⁷ Among other recommendations, the NAS argued that “***cancer and noncancer responses [to chemical exposures] be assumed to be linear as a default ***.”⁵⁸

The MOE approach presented in the methylene chloride draft risk evaluation provides a bright-line, yes/no approach to risk and fails to provide a measure of population risk at a given exposure level. This approach limits the assessment’s utility for risk managers, particularly when comparing options for substitution and conducting risk-benefit comparisons.

The National Academy of Sciences (NAS) Committee on Improving Risk Analysis Approaches Used by the U.S. EPA concluded “separation of cancer and noncancer outcomes in dose response analysis is artificial because noncancer endpoints can occur without a threshold or low dose nonlinearity at the population level.”⁵⁹ The Committee further stated that background exposures and underlying disease processes can contribute to background risk and lead to linearity at population doses of concern.

EPA should implement the recommendations of the NAS and develop a unified approach to presenting dose-specific population risks for both cancer and noncancer endpoints.

5. EPA’s human exposure assessment raises significant questions and concerns.

A. EPA’s unwarranted assumption of respirator use obscures the full extent of unreasonable risk to workers posed by inhalation of methylene chloride.

i. Context and summary

EPA’s presentation of its risk determinations in Table 5-1 (pp. 432-475) dramatically understates the extent of actual unreasonable inhalation risk to workers it has identified.

As discussed elsewhere in the comments (section 1.B.), EPA has adopted a flawed assumption – absent any empirical evidence to support it – that workers under many conditions of use of methylene chloride will always wear effective personal protective equipment (PPE).

EPA’s application of this assumption to workers under the various conditions of use of methylene chloride is largely masked by EPA’s presentation of its risk determinations in Table 5-1, but EDF has conducted a detailed analysis that demonstrates that this assumption is 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.

⁵⁷ NAT’L RESEARCH COUNCIL, SCIENCE AND DECISIONS: ADVANCING RISK ASSESSMENT (2009), <https://www.ncbi.nlm.nih.gov/books/NBK214630/>.

⁵⁸ *Id.* at chp. 5, p. 180.

⁵⁹ *Id.* at chp. 5, p. 177.

By poring through the dozens of detailed tables in the bowels of its draft risk evaluation (Chapter 4), we were able to discern the levels of risk EPA found for various conditions of use of methylene chloride. EPA's tables show: 1) the risk levels EPA calculated *before* it applied its assumption regarding PPE use; then 2) whether EPA's assumption of PPE could make enough risk go away so that EPA could claim there is no unreasonable risk; and 3) if so, what degree of efficiency of respirators EPA had to assume would be used.

Our examination revealed the following:

- There are only two kinds of scenarios under which EPA did find unreasonable inhalation risk to workers:
 - **Scenarios where the risks EPA calculated are so high that it could not make them go away even *after* assuming that workers would always use the most protective respirator that EPA considered.** This would require use of a highly efficient (and highly cumbersome) supplied-air respirator with an “assigned protection factor” (APF) of 25 or 50, i.e., one that reduces air concentrations by 25- or 50-fold.
 - **Scenarios where EPA could not plausibly assume *any* use of respirators by the exposed persons.** These include workers under conditions of use like recycling, textile finishing, car care, and paint and coating removal.
- With one exception, for all conditions of use where EPA found there was not unreasonable inhalation risk to workers, in order to reach that finding, **EPA had to assume that all of the workers were using respirators.**
 - The exception is distribution, where EPA failed to conduct any actual analysis of risks; see section 9.C.
- Even where EPA did find unreasonable inhalation risk to workers, **EPA has grossly understated both the extent and magnitude of those risks.** We present a detailed analysis of these conditions of use below.

Put another way: For every one of the conditions of use where EPA could assume respirators might plausibly be used, EPA either:

- avoided identifying an unreasonable risk from inhalation exposure *only* by assuming universal, effective use of respirators; or
- found unreasonable risk even with the use of such respirators – but by relying on the risk estimate calculated assuming the PPE, grossly understated both the extent and magnitude of the risk.

For *both* the “unreasonable risk” and “no unreasonable risk” determinations, EPA's unwarranted approach raises major concerns. 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. If EPA does find unreasonable risk even with its PPE assumptions, by understating the extent and magnitude of that risk, any subsequent regulation EPA promulgates under TSCA will be under-protective of workers.

ii. Detailed analysis of COUs where EPA assumed routine use of respirators

EPA assumed routine use of inhalation PPE (respirators) for 29 of its 65 COUs.⁶⁰ Our analysis of these COUs found the following:

FINDING 1: *For each one of these 29 COUs, at least one of the risk estimates for the COU⁶¹ EPA considered for its risk determination was changed due to EPA's assumed use of respiratory PPE.* For each such risk estimate – but for that assumption – the estimate would have indicated either:

- an unreasonable risk relative to EPA's risk benchmark; or
- a higher unreasonable risk than EPA identified.

FINDING 2: Across the 29 COUs, *EPA's assumption of respiratory PPE use either "eliminated" or "understated" 74% of the risk estimates* calculated for the COUs. That is, absent EPA's assumption of PPE use, for each such risk estimate EPA either:

- would have identified an unreasonable risk where it has not (hence the risk estimate was effectively "eliminated" from consideration); or

⁶⁰ For 35 of the 65 conditions of use, in each of their entries in Table 5-1 EPA stated: "[it] does not expect routine use of respiratory PPE sufficient to mitigate risk." Therefore, even though EPA sometimes calculated risk estimates for these conditions of use with respiratory PPE in its risk estimation tables in Chapter 4 of the draft risk evaluation, EPA's final risk determinations were not *intended* to be based on an assumption of respiratory PPE use (but see section 9.A.v.b. for cases where EPA, possibly inadvertently, invoked respiratory PPE use after indicating it did not expect PPE to be used). This analysis focuses on the remaining 29 COUs where EPA did not intend to assume use of respiratory PPE by workers.

⁶¹ The 10 individual risk estimates, not all of which were calculated for each COU, are:

- Acute, 8-hr, high end
- Acute, 8-hr, central tendency
- Acute, 15-min, high end
- Acute, 15-min, central tendency
- Acute, 1-hr, high end
- Acute, 1-hr, central tendency
- Chronic, high end
- Chronic, central tendency
- Cancer, high end
- Cancer, central tendency

- would have found an even higher unreasonable risk than it has (hence the risk estimate was “understated”).⁶²

Details: See the description and Table B below and the “inhalation” tab of the Excel spreadsheet EDF submitted along with these comments.⁶³

Of the 29 COUs, EPA made a final risk determination that 19 of them presented unreasonable risk to workers, while 10 did not. Below we separately present the results of our analysis for these two cases.

1. Cases where EPA found unreasonable risk to workers (19 of 29 COUs):⁶⁴

Even though EPA ultimately made a final determination of unreasonable risk to workers, for all 19 of these cases, at least one of the risk estimates for each COU was changed due to EPA’s assumed use of respiratory PPE to eliminate from consideration or understate that risk estimate.

- a. Cases where a given EPA non-cancer risk estimate indicates unreasonable risk relative to EPA’s risk benchmarks *even assuming use of respiratory PPE* (“Yes w/ PPE”⁶⁵).

Risk estimate:	# of COUs with risk estimates understated due to PPE:
• Yes w/ PPE:	<u>19 of 19 unique COUs overall</u>
○ Acute:	<u>19 of 19 unique COUs for acute</u>
• 8-hr:	
○ High-end:	19 of 19
○ Central tendency:	4 of 19
• 15-min	
○ High-end:	0 of 19
○ Central tendency:	0 of 19
• 1-hr	

⁶² Across the 29 COUs, EPA provided a total of 203 separate risk estimates. EPA did not calculate all 10 risk estimates for each COU; on average, it calculated 7 risk estimates per COU. On average, 5.2 of these 7 risk estimates were either “eliminated” or “understated” due to EPA’s respiratory PPE assumption. Across the 29 COUs, this amounted to 151 of the 203 risk estimates, or 74%.

⁶³ See Appendix B.

⁶⁴ These cases represent instances where EPA’s risk estimate *underestimates* the risk to workers even though EPA found unreasonable risk.

⁶⁵ The phrase in quotation marks refers to the matching phrase used in the cell entries in the chart below and on the “inhalation tab of the attached spreadsheet.

- High-end: 0 of 19
 - Central tendency: 0 of 19
- Chronic: 19 of 19 unique COUs for chronic
 - High-end: 19 of 19
 - Central tendency: 3 of 19

b. Cases where a given EPA non-cancer risk estimate indicates unreasonable risk relative to EPA's risk benchmarks *before but not after EPA assumed use of respiratory PPE* ("No w/ PPE").

Risk estimate: # of COUs with risk estimates eliminated due to PPE:

- No w/ PPE: 16 of 19 unique COUs overall
 - Acute: 15 of 19 unique COUs for acute
 - 8-hr:
 - High-end: 0 of 19
 - Central tendency: 15 of 19
 - 15-min
 - High-end: NA
 - Central tendency: NA
 - Point estimate: 11 of 19
 - NC: 8 of 19
 - 1-hr
 - High-end: 0 of 19
 - Central tendency: 0 of 19
 - NC: 19 of 19
 - Chronic: 16 of 19 unique COUs for chronic
 - High-end: 0 of 19
 - Central tendency: 16 of 19

c. Cases where a given EPA cancer risk estimate indicates unreasonable risk relative to EPA's 10^{-4} risk benchmark *before but not after EPA assumed use of respiratory PPE*.⁶⁶

Risk estimate: # of COUs with risk estimates eliminated due to PPE:

- Cancer: 19 of 19 unique COUs for cancer
 - High-end: 19 of 19

⁶⁶ These are cases where, in Table B below, the values in the "No PPE" column for cancer are ≤ 4 , and the values in the "PPE" column for cancer are > 4 . In other words, the values before PPE is assumed exceed EPA's cancer risk benchmark of 10^{-4} while the values after PPE is assumed do not.

- Central tendency: 7 of 19

2. Cases where EPA found no unreasonable risk to workers (10 of 29 COUs):⁶⁷

In all 10 cases, at least one risk estimate was changed due to EPA's assumed use of respiratory PPE to eliminate that risk estimate from consideration.

- a. Cases where a given EPA non-cancer risk estimate indicates unreasonable risk relative to EPA's risk benchmarks *before but not after EPA assumed use of respiratory PPE* ("No w/ PPE").

Risk estimate:	# of COUs with risk estimates eliminated due to PPE:
• No w/ PPE:	<u>10 of 10 unique COUs overall</u>
○ Acute:	<u>10 of 10 unique COUs for acute</u>
• 8-hr:	
○ High-end:	9 of 10
○ Central tendency:	1 of 10
• 15-min	
○ High-end:	3 of 10
○ Central tendency:	1 of 10
○ Point estimate:	4 of 10
○ NC:	3 of 10
• 1-hr	

⁶⁷ These cases represent instances where EPA's risk estimate led it to *avoid identifying an unreasonable risk* it should have identified. These 10 COUs are:

- Manufacturing
 - Intermediate in industrial gas manufacturing (e.g., manufacture of fluorinated gases used as refrigerants)
 - Intermediate for pesticide, fertilizer, and other agricultural chemical manufacturing
 - Petrochemical manufacturing
 - Intermediate for other chemicals
- Repackaging:
 - Solvents (which become part of product formulation or mixture)
 - All other chemical product and preparation manufacturing
- Laboratory chemicals - all other chemical product and preparation manufacturing
- Plastic and rubber products (plastic manufacturing)

- High-end: 3 of 10
 - Central tendency: 3 of 10
 - NC: 6 of 10
 - Chronic: 9 of 10 unique COUs for chronic
 - High-end: 9 of 10
 - Central tendency: 4 of 10
- b. Cases where a given EPA cancer risk estimate indicates unreasonable risk relative to EPA's 10^{-4} risk benchmark *before but not after EPA assumed use of respiratory PPE*.⁶⁸

Risk estimate: # of COUs with risk estimates eliminated due to PPE:

- Cancer: 2 of 10 unique COUs for cancer
 - High-end: 2 of 10
 - Central tendency: 0 of 10

⁶⁸ These are cases where, in Table B below, the values in the “No PPE” column for cancer are ≤ 4 , and the values in the “PPE” column for cancer are > 4 . In other words, the values before PPE is assumed exceed EPA's cancer risk benchmark of 10^{-4} while the values after PPE is assumed do not.

Table B: Effect of EPA's PPE Assumption on Inhalation Risk Estimates for Workers
(A key explaining the terminology used is on the last page)

				Cancer				Acute (CNS effects)						Chronic (Liver effects)	
				High end		Central		8 hour		15 minute		1 hour			
Life cycle stage	Category	Subcategory	Did EPA find unreasonable risk?	No PPE	PPE	No PPE	PPE	High end	Central	High end	Central	High end	Center	High end	Central
Manufacturing	Domestic manufacturing	Manufacturing	No (both)	6	8	7	9	No w/o PPE	No w/o PPE	No w/ PPE	No w/o PPE	No w/o PPE	No w/o PPE	No w/o PPE	No w/o PPE
	Import	Import	Yes (O)	5	NC	6	NC	No w/ PPE	No w/o PPE	NC	NC	No w/ PPE	No w/ PPE	No w/ PPE	No w/ PPE
Processing	Processing as a reactant	Intermediate in industrial gas manufacturing	No (both)	6	NC	7	NC	No w/ PPE	No w/o PPE	No w/ PPE*	No w/ PPE*	NC	NC	No w/ PPE	No w/o PPE
		Intermediate for pesticide, fertilizer, and other ag. chem. manufacturing	No (both)	6	NC	7	NC	No w/ PPE	No w/o PPE	No w/ PPE*	No w/ PPE*	NC	NC	No w/ PPE	No w/o PPE
		Petrochemical manufacturing	No (both)	6	NC	7	NC	No w/ PPE	No w/o PPE	No w/ PPE*	No w/ PPE*	NC	NC	No w/ PPE	No w/o PPE
		Intermediate for other chemicals	No (both)	6	NC	7	NC	No w/ PPE	No w/o PPE	No w/ PPE*	No w/ PPE*	NC	NC	No w/ PPE	No w/o PPE
	Incorporated into formulation, mixture, or reaction product	Solvents: cleaning/degreasing	Yes (both)	3	5	5	6	Yes w/ PPE	No w/ PPE	No w/ PPE*	No w/ PPE*	NC	NC	Yes w/ PPE	No w/ PPE
		Solvents: part of product formulation	Yes (both)	3	5	5	6	Yes w/ PPE	No w/ PPE	No w/ PPE*	No w/ PPE*	NC	NC	Yes w/ PPE	No w/ PPE
		Propellants: all other chemical product and preparation manufacturing	Yes (both)	3	5	5	6	Yes w/ PPE	No w/ PPE	No w/ PPE*	No w/ PPE*	NC	NC	Yes w/ PPE	No w/ PPE
		Propellants: plastics product manufacturing	Yes (both)	3	5	5	6	Yes w/ PPE	No w/ PPE	No w/ PPE*	No w/ PPE*	NC	NC	Yes w/ PPE	No w/ PPE

Table B: Effect of EPA's PPE Assumption on Inhalation Risk Estimates for Workers

(A key explaining the terminology used is on the last page)

				Cancer				Acute (CNS effects)						Chronic (Liver effects)	
				High end		Central		8 hour		15 minute		1 hour			
Life cycle stage	Category	Subcategory	Did EPA find unreasonable risk?	No PPE	PPE	No PPE	PPE	High end	Central	High end	Central	High end	Center	High end	Central
Processing	Incorporated into formulation, mixture, or reaction product	Paint additives and coating additives not described by other codes for CBI industrial sector	Yes (both)	3	5	5	6	Yes w/ PPE	No w/ PPE	No w/ PPE*	No w/ PPE*	NC	NC	Yes w/ PPE	No w/ PPE
		Laboratory chemicals for all other chemical product and preparation manufacturing	Yes (both)	3	5	5	6	Yes w/ PPE	No w/ PPE	No w/ PPE*	No w/ PPE*	NC	NC	Yes w/ PPE	No w/ PPE
		Laboratory chemicals	Yes (both)	3	5	5	6	Yes w/ PPE	No w/ PPE	No w/ PPE*	No w/ PPE*	NC	NC	Yes w/ PPE	No w/ PPE
		Processing aid, not otherwise listed for petrochemical manufacturing	Yes (both)	3	5	5	6	Yes w/ PPE	No w/ PPE	No w/ PPE*	No w/ PPE*	NC	NC	Yes w/ PPE	No w/ PPE
		Adhesive and sealant chemicals in adhesive manufacturing	Yes (both)	3	5	5	6	Yes w/ PPE	No w/ PPE	No w/ PPE*	No w/ PPE*	NC	NC	Yes w/ PPE	No w/ PPE
		Oil and gas drilling, extraction, and support activities	Yes (both)	3	5	5	6	Yes w/ PPE	No w/ PPE	No w/ PPE*	No w/ PPE*	NC	NC	Yes w/ PPE	No w/ PPE
	Repackaging	Solvents (which become part of product formulation or mixture)	Yes (O)	5	NC	6	NC	No w/ PPE	No w/o PPE	NC	NC	No w/ PPE	No w/ PPE	No w/ PPE	No w/ PPE
		All other chemical product and preparation manufacturing	Yes (O)	5	NC	6	NC	No w/ PPE	No w/o PPE	NC	NC	No w/ PPE	No w/ PPE	No w/ PPE	No w/ PPE

Table B: Effect of EPA's PPE Assumption on Inhalation Risk Estimates for Workers
(A key explaining the terminology used is on the last page)

				Cancer				Acute (CNS effects)						Chronic (Liver effects)	
				High end		Central		8 hour		15 minute		1 hour			
Life cycle stage	Category	Subcategory	Did EPA find unreasonable risk?	No PPE	PPE	No PPE	PPE	High end	Central	High end	Central	High end	Center	High end	Central
Industrial/ commercial uses	Solvents (cleaning or degreasing)	Batch vapor degreaser (e.g., open-top, closed-loop)	Yes (both)	4	5	5	6	Yes w/ PPE	No w/ PPE	NC	NC	NC	NC	Yes w/ PPE	No w/ PPE
	Solvents (cleaning or degreasing)	In-line vapor degreaser	Yes (both)	4	5	4	5	Yes w/ PPE	Yes w/ PPE	NC	NC	NC	NC	Yes w/ PPE	No w/ PPE
		Cold cleaner	Yes (both)	4	5	4	6	Yes w/ PPE	No w/ PPE	NC	NC	NC	NC	Yes w/ PPE	No w/ PPE
	Paints and coatings including paint and coating removers	Adhesive/caulk removers	Yes (both)	3	5/5	4	5/5	Yes w/ PPE	Yes w/ PPE	NC	NC	NC	NC	Yes w/ PPE	Yes w/ PPE
	Solvents: part of product formulation or mixture	All other chemical product and preparation manufacturing	Yes (both)	3	5	5	6	Yes w/ PPE	No w/ PPE	No w/ PPE*	No w/ PPE*	NC	NC	Yes w/ PPE	No w/ PPE
	Processing aid not otherwise listed	In multiple manufacturing sectors	Yes (both)	4	5	4	5	Yes w/ PPE	Yes w/ PPE	NC	NC	NC	NC	Yes w/ PPE	Yes w/ PPE
	Propellants and blowing agents	Flexible polyurethane foam manufacturing	Yes (both)	4	5/5	4	6/6	Yes w/ PPE	No w/ PPE	NC	NC	NC	NC	Yes w/ PPE	No w/ PPE
	Other uses	Laboratory chemicals - all other chemical product and preparation manufacturing	No (both)	4	6	6	8	No w/ PPE	No w/o PPE	No w/ PPE	No w/o PPE	NC	NC	No w/ PPE	No w/o PPE
		Plastic and rubber products (plastic manufacturing)	Yes (O)	4	6	6	7	No w/ PPE	No w/ PPE	No w/ PPE	No w/ PPE	NC	NC	No w/ PPE	No w/ PPE

Table B: Effect of EPA's PPE Assumption on Inhalation Risk Estimates for Workers

(A key explaining the terminology used is on the last page)

				Cancer				Acute (CNS effects)						Chronic (Liver effects)	
				High end		Central		8 hour		15 minute		1 hour			
Life cycle stage	Category	Subcategory	Did EPA find unreasonable risk?	No PPE	PPE	No PPE	PPE	High end	Central	High end	Central	High end	Center	High end	Central
Industrial/ commercial uses	Other uses	Plastic and rubber products (cellulose and triacetate film production)	Yes (both)	4	5	4	5	Yes w/ PPE	Yes w/ PPE	NC	NC	NC	NC	Yes w/ PPE	Yes w/ PPE
		Functional fluids (closed systems) in pharmaceutical and medicine manufacturing	Yes (both)	3	5	4	6	Yes w/ PPE	No w/ PPE	NC	NC	NC	NC	Yes w/ PPE	No w/ PPE
KEY:															
Column 4: Asks whether EPA found unreasonable risk to workers and ONUs only (W = workers; O = ONUs)															
<i>Cancer:</i>						<i>Acute and Chronic:</i>									
· An asterisk indicates EPA does not expect PPE to be used for the condition of use						· No w/o PPE = EPA's risk estimate was above the benchmark MOE even assuming no PPE use (yellow)									
· In some instances, EPA calculated estimates based on use of either of two types of respirators (APF = 25 or 50); the two resulting values are separated by a slash						· No w/ PPE = EPA's risk estimate was below the benchmark MOE in the absence of PPE, but EPA made a finding of no risk based on a presumption of PPE use (orange)									
· The numeric values indicate which benchmark would have been exceeded: e.g., "4" is $\geq 10^{-4}$ but $< 10^{-3}$, "5" is $\geq 10^{-5}$ but $< 10^{-4}$, "6" is $\geq 10^{-6}$ but $< 10^{-5}$.						· Yes w/ PPE = EPA's risk was below the benchmark MOE even assuming PPE was used (blue)									
Yellow = risk estimate is $< 10^{-4}$ w/o PPE						· An asterisk indicates that EPA only calculated a "point" estimate									
Orange = risk estimate is $< 10^{-4}$ w/ PPE						· NC means EPA did not calculate that scenario									
Green = risk estimate is $\geq 10^{-4}$ w/o PPE															
· NC means EPA did not calculate that scenario															

B. EPA's unwarranted assumption of glove use obscures the full extent of unreasonable risk to workers posed by dermal exposure to methylene chloride.

As discussed elsewhere in the comments (section 1.B.), EPA has adopted a flawed assumption – absent any empirical evidence to support it – that workers under many conditions of use of methylene chloride will always wear effective personal protective equipment (PPE), including gloves.

In assessing risks from dermal exposures to workers, EPA analyzed 23 occupational exposure scenarios (pp. 344-49). For all 23 scenarios, EPA found that the exposures, absent glove use, present unreasonable risks for both acute and chronic, non-cancer health effects. This means that EPA found that *any* worker not wearing gloves in any of these scenarios would experience an unreasonable risk.

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 a MOE falling below EPA's benchmarks MOEs, indicating unreasonable risk.

Below are the number of risk estimates indicating unreasonable risk that EPA eliminated from consideration through its dermal PPE assumption:

- Acute
 - Central tendency:
 - Eliminated 23 out of 23 unreasonable risk estimates by assuming use of gloves with a PF of 5
 - High end:
 - Eliminated 15 out of 23 by relying on PF 5 gloves
 - Eliminated the remaining 8 of the 23 by relying on PF 10 gloves
- Chronic
 - Central tendency:
 - Eliminated 23 out of 23 by relying on PF 5 gloves
 - High end:
 - Eliminated 8 of 23 by relying on PF 10 gloves
 - Eliminated 8 more of the 23 by relying on PF 20 gloves

- Eliminated the remaining 7 because, although EPA could not assume use of PF 20 gloves, with PF 10 gloves the MOEs were “very nearly” at the benchmark MOE⁶⁹

The “dermal” tab of the spreadsheet EDF attached to these comments provides the breakdown for each scenario.⁷⁰

C. EPA has underestimated occupational and consumer exposures.

i. EPA has failed to consider workers’ combined exposure from multiple pathways.

EPA never considers the combined risks from the inhalation and dermal exposures it calculates – even though many workers could readily experience exposures by both routes, including over the same time period. For example, in the context of estimating dermal exposure, the agency states that “[e]xposures to skin would be expected to evaporate rapidly (0.06 mol/s) based on physical chemical properties including vapor pressure, water solubility and log Kow” (p. 167), which would lead to increased concentration in the air in the immediate vicinity of the dermally exposed worker. Because both inhalation and dermal exposure result in systemic distribution of methylene chloride, (p. 217) it is essential to evaluate exposures from both of these routes in combination, including simultaneously, to assess total body burden and the associated effects.

EPA does acknowledge in the draft risk evaluation that workers and consumers may experience both inhalation and dermal exposures – and indicates that the agency considered adding them together. However, EPA dismisses the approach due to “uncertainties” associated with its PBPK model:

The available PBPK models lack a dermal compartment and therefore a PBPK model for aggregating inhalation and dermal exposures is not reasonably available. Aggregating inhalation and dermal exposures without the use of a PBPK model would introduce additional uncertainties and was not included here. EPA chose not to employ simply additivity of exposure pathways at this time within a condition of use because of the uncertainties present in the current exposure estimation procedures. (p. 387)

EPA acknowledges that its approach “may lead to an underestimate of exposure” but ultimately dismisses the concern by assuming that the dominant exposure pathway is inhalation due to methylene chloride’s physical-chemical properties. This rationale is insufficient, especially 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 PF 5 or 10 (pp. 344-349).

⁶⁹ See section 9.A.iv. for a full critique of EPA’s approach.

⁷⁰ See Appendix B.

Our concern is reinforced by the comments of several SACC members made during both the 1,4-dioxane and 1-bromopropane peer review meetings, who called on the agency to combine the inhalation and dermal exposures.

Another concern raised by a SACC member is salient for methylene chloride as well: EPA has ignored all non-occupational baseline exposures workers experience, due to its exclusion of all exposures via environmental releases to air, water, and land. The SACC member argued that the agency at least needs to take these into account as baseline exposures for workers, even if the agency persists in not considering them as arising from conditions of use it has included within the scope of the risk evaluation. In other words, even if the agency does not intend to assess risks from environmental releases of methylene chloride through the air, water, and land (due to its assertions as to the adequacy of actions taken under other statutes), EPA cannot ignore these real-world exposures when assessing the risk methylene chloride presents to an individual.

ii. EPA may have underestimated exposure to ONUs.

We support EPA's decision to assume that occupational non-users (ONUs) will not wear respirators. Beyond the concerns we raised earlier with assumptions that workers handling a chemical will consistently wear PPE and that it will be universally effective, it would be far more unrealistic to assume that ONUs would wear any PPE. This point was raised repeatedly by SACC members during their 1,4-dioxane peer review meeting.

Nevertheless, EPA may still have underestimated exposure to ONUs in several ways. First, as discussed in detail in section 9.A.iii., EPA assumes central tendency exposures for ONUs in any case where it does not have monitoring data or modeling specific to ONUs.

Second, where EPA does have data to estimate exposure of ONUs specifically, the agency assumes that they are only present in the "far field zone" – i.e., outside of the "near field" workers' zone. (p. 373) However, ONUs may not stay within the "far field zone." Several SACC members raised this concern during the 1-BP peer review meeting. For example, a SACC member with industrial hygiene experience noted that workers and ONUs may regularly pass into each other's space, e.g., to communicate or otherwise interact. EPA acknowledges this limitation: "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," (p. 371), and later acknowledges that its assumption may lead to underestimating exposure: "The assumption that ONUs are present only in the far-field could result in underestimates for ONUs present in the near-field." (p. 373). But EPA then ignores this potential in characterizing ONU exposures.

iii. EPA has failed to explain or justify its assumption of one exposure event per day.

In its dermal exposure assessment, EPA assumes one exposure event per day for both workers (pp. 165, 375) and consumers (p. 173). EPA provides little justification for these assumptions.

Yet, for workers, given the typical 8-hour (or longer) work day and the repetition common in many jobs, it seems far more likely that workers would regularly engage in activities that could result in multiple exposure events per day. EPA seems to recognize this when it states that its assumption “likely underestimates exposure as workers often come into repeat contact with the chemical throughout their work day.” (pp. 165, 375) But EPA then fails to account for this underestimation or provide any sort of uncertainty analysis.

With regards to consumers, EPA also assumes a single exposure event per day, although it does take into account varying durations of exposure. (pp. 168, 177-78) But EPA also fails to assess any chronic exposures despite acknowledging they are expected to occur (p. 169): “For all product scenarios, both acute and chronic exposures were expected to occur, but only acute exposures are evaluated here.”

EPA has not address the potential that consumers who are “do-it-yourselfers” may be exposed more frequently. This stands in contrast to the agency’s draft risk evaluation for 1-bromopropane, which acknowledged this subpopulation (but then failed to analyze it):

This assumption may result in underestimating the exposure of certain consumer users, in particular those consumers who may be do-it-yourselfers who may use products more frequently or may use more than one product within a single day. There is a medium uncertainty associated with this assumption because of the possible of underestimating exposure of frequent use or multi-product users. (draft risk evaluation for 1-bromopropane, p. 130)

EPA’s assumption about consumer exposure seems likely to significantly underestimate the risks they face. At the very least, EPA needs to conduct a sensitivity analysis regarding these assumptions in the context of this risk evaluation, which is different than the sensitivity analysis EPA indicates was done on the model itself (p. 179).

iv. EPA’s assessment of dermal exposure likely underestimates exposure due to its crude assumptions about glove use and efficacy.

As noted above, section 1.B., EPA does not appear to have any actual data on glove use and efficacy, which is necessary to accurately assess dermal exposure. EPA states:

Regarding glove use, 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.
(p. 110)

Also as noted above, EPA acknowledges in the draft risk evaluation (p. 110) that gloves are likely to provide only limited protection from methylene chloride, given that the chemical can break through gloves made of certain materials.

EPA recognizes the potential for occlusion, whereby glove use can *increase* skin exposure, and 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).⁷¹ That supplemental document calculated exposure in occluded scenarios for the occupational exposure scenarios in Bin 2 (Industrial), Bin 3 (Commercial), and Bin 4 (Commercial), finding exposures that are 8-37 times higher than the no-glove scenarios.⁷²

However, it appears that the exposure estimates under occluded conditions are not actually incorporated into the risk characterizations and risk determinations at all. For example, when one compares Table 2-85 in the draft risk evaluation (p. 165) to 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.

Instead, the agency simply uses default glove protection factors, ignoring the elevated dermal exposures of workers in occluded scenarios. More specifically, the agency assumes fixed protection factors (PFs) of 5x, 10x, and 20x, which do not appear to be supported by any empirical data that account for the complexities of glove use in the real world. In fact, EPA itself states that the glove protection factors are ““what-if” assumptions and are uncertain” (p. 166). While EPA acknowledges that the level of protection varies greatly with different glove materials, even recommending specific material types (pp. 594-597), EPA does not integrate any of this information into its dermal exposure assessment. Further, the agency fails to acknowledge the uncertainties and deficiencies in its glove use assumptions in the Risk Determination section of the risk evaluation.

⁷¹ U.S. EPA, *Draft Risk Evaluation for Methylene Chloride (Dichloromethane, DCM) DCM Supplemental File: Supplemental Information on Releases and Occupational Exposure Assessment CASRN: 75-09-2i* (Oct. 2019), <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0437-0019>.

⁷² For Bin 3, “Adhesives and Caulk Removers/Spot Cleaning,” EPA calculated an occluded exposure of 2,022 mg/day compared to 260 mg/day for high end exposure without gloves (2,022/260 = **7.77**). For Bin 2, EPA calculated an occluded exposure of 2,247 mg/day compared to 60 mg/day for central tendency without gloves (2,247/60 = **37.45**).

During both the 1,4-dioxane and 1-BP SAAC peer review meetings, a SACC member who is a dermal exposure expert expressed his concern with EPA's approach, which EPA has repeated for methylene chloride. He noted that glove testing is typically conducted in a lab under ideal conditions – without an actual human hand present. However, in the real world, an insufficiently trained or attentive user may contaminate a glove, leading to occlusion and higher exposure. Likewise, permeable gloves may enable the chemical to be absorbed through the glove, while preventing or slowing evaporation. 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 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. The unstated, but highly questionable, premise seems to be that if the most protective gloves potentially available can be assumed to provide a PF that reduces risk to below the benchmark, then EPA can conclude there is no unreasonable risk. 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.

D. EPA inappropriately relies solely on occupational exposure data from the Halogenated Solvents Industry Alliance for two conditions of use and ignores available data from OSHA to support its determinations of no unreasonable risk.

OSHA has collected a tremendous amount of data on methylene chloride exposure since the mid-1980s. Our own search using the OSHA Chemical Exposure Health Data tool⁷³ yielded 11,272 air samples for methylene chloride dated as recently as June 2019.

However, instead of relying on OSHA's data for the "Manufacturing" and "Processing as a Reactant" conditions of use, EPA relies solely on data submitted by the Halogenated Solvents Industry Alliance (HSIA) during the problem formulation stage, and ultimately finds "no unreasonable risk" for these two COUs.⁷⁴ HSIA is the main trade association for manufacturers of methylene chloride, and, as such, it has a strong vested interest in EPA finding no unreasonable risk from the chemical. For example, the data submitted by HSIA are part of its comments in which it also argues, among other things, that methylene chloride is not

⁷³ CHEMICAL EXPOSURE HEALTH DATA, <https://www.osha.gov/opengov/healthsamples.html> (last visited Nov. 26, 2019).

⁷⁴ Halogenated Solvents Industry Alliance Problem Formulation Comments on Methylene Chloride (Aug. 2018), <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0742-0103>.

carcinogenic.⁷⁵ This vested interest calls into question the reliability and completeness of the data voluntarily submitted by HSIA.

In its systematic review process, EPA rated the 2018 HSIA data as 1.6, or “High.”⁷⁶ In doing so, EPA made some questionable decisions. First, EPA assigned the data a score of “1” for Geographic Scope because the data come from U.S. facilities. However, it appears that the data represent only four manufacturing facilities (as the HSIA comment document separately lists samples from Companies A, B, C, and D), and it is unclear how representative of the entire country the data are.⁷⁷ Second, as EPA acknowledges, HSIA has not provided a standard description of the methods used to collect the data or to analyze the samples. EPA assigned the 2018 data a “3” for Methodology due to “methods not specified.” However, 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. Third, and more broadly, EPA’s systematic review protocol does not take into consideration the potential for bias based on the data source. Finally, EPA has not adequately compared HSIA’s data to that available through OSHA; see further discussion below. EPA provides insufficient justification for its exclusive reliance upon this potentially biased data without independent validation and quality assurance reporting.

⁷⁵ In fact, EPA’s Integrated Risk Information System (IRIS) determined that methylene chloride is “likely to be carcinogenic in humans” based on a mutagenic mode of action and the U.S. National Toxicology Program under the Department of Health and Human Services, in its 14th Report on Carcinogens, determined that DCM is “reasonably anticipated to be a human carcinogen.” See U.S. EPA, *Toxicological Review of Dichloromethane (Methylene Chloride)* (2011), https://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/0070tr.pdf; Nat’l Toxicology Program, *Substances Listed in the Fourteenth Report on Carcinogens*, https://ntp.niehs.nih.gov/ntp/roc/content/listed_substances_508.pdf.

⁷⁶ This rating applies to the HSIA data dated 2018, the review of which appears on p. 356 of Systematic Review Supplemental File: Data Quality Evaluation of Environmental Release and Occupational Exposure Data, at https://www.epa.gov/sites/production/files/2019-10/documents/4_draft_systematic_review_supplemental_file_data_quality_evaluation_of_environmental_releases_and_occupational_exposure_data.pdf.

⁷⁷ EPA’s 2016 Chemical Data Reporting data (see 2016 CHEMICAL DATA REPORTING RESULTS, <https://www.epa.gov/chemical-data-reporting/2016-chemical-data-reporting-results> (last visited Nov. 26, 2019)) for methylene chloride identified by name and location four U.S. facilities, but also listed records for six additional facilities for which the submitter had claimed as confidential business information (CBI) whether the facility produced or imported methylene chloride. In addition, for four additional facilities, EPA has withheld that information. Moreover, as EPA noted on p. 40, “only companies that manufactured or imported 25,000 pounds or more of methylene chloride at each of their sites during the 2015 calendar year were required to report information under the CDR rule.” So it is not possible to discern from these data how many facilities manufacture methylene chloride in the U.S.

In 2017, Dr. Adam Finkel, a former OSHA official, submitted comments to the docket on EPA's proposed section 6 rule on methylene chloride in paint and coating removal that included a robust OSHA dataset of personal air samples from 1984-2016.⁷⁸ While EPA used these data for some conditions of use in the draft risk evaluation, the agency did not utilize the data for the Manufacturing or Processing as a Reactant conditions of use or do any comparison with the HSIA data it chose to use, even though the OSHA data generally indicate much higher levels of exposure than the HSIA data. Furthermore, as illustrated by Table 2-84 of the draft risk evaluation (pp. 163-164), EPA's worker exposure estimates are lower for Manufacturing and Processing as a Reactant than for any other conditions of use – in some cases by several orders of magnitude.

Further, based on the systematic review supplemental file on environmental release and occupational exposure data, it appears that EPA did not even obtain and examine the OSHA data directly, but instead relied on the data submitted indirectly from Dr. Finkel. It is EDF's understanding that Dr. Finkel submitted a Freedom of Information Act (FOIA) request, through which he received more complete data (up until 2016) than are available through OSHA's public website. However, EPA is mandated under TSCA to consult with OSHA; there is no reason that the agency could not and should not have acquired data directly from OSHA. This have allowed EPA to take advantage of more recent data (post-2016).

While there may be a role for the data submitted by HSIA in the risk evaluation, it is inappropriate for the agency to completely ignore data collected and maintained by OSHA. In finalizing the risk evaluation, EPA must acquire all of the relevant OSHA data in order to comply with its requirement to consider reasonably available information and the best available science, as required under TSCA section 26.

E. EPA inappropriately characterizes and relies on the OSHA Permissible Exposure Limit.

EPA inappropriately invokes the OSHA Permissible Exposure Limit (PEL) as a benchmark. Specifically, EPA compares each occupational exposure estimate to the PEL as well as the OSHA Short-Term Exposure Limit (STEL) in section 2.4.1.2. For example, under the Manufacturing condition of use, EPA states: "Both the central tendency and high-end 8-hr TWA exposure concentrations for this scenario are at least one order of magnitude below the OSHA Permissible Exposure Limit (PEL) value of 87 mg/m³ (25 ppm) as an 8-hr TWA." This comparison is inappropriate as it implies that the PEL is a suitable risk benchmark.

⁷⁸ Comment by Dr. Adam M. Finkel on Regulation of Certain Uses under Toxic Substances Control Act: Methylene Chloride and N-Methylpyrrolidone at 3 (May 19, 2017), <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0231-0536>.

In fact, OSHA's PEL of 25 ppm is not a health-protective standard. It was last updated in 1997 – over 20 years ago – and EPA's proposed section 6 rule on use of methylene chloride and NMP in paint and coating removal concluded that OSHA's PEL is substantially higher than the levels at which EPA identified unreasonable risk.⁷⁹ Furthermore, within the context of paint and coating removal exposures, OSHA itself has indicated that the PEL would be insufficient to protect workers from the risks.⁸⁰

As a further indication of the inadequacy of OSHA's PEL, in the course of developing the proposed rule, EPA developed a recommendation for an Existing Chemical Concentration Limit, or "ECEL"⁸¹ as a more current benchmark for workplace exposures. EPA developed a recommended value of 1.3 ppm (8-hour time weighted average), which is nearly 20-fold lower than OSHA's PEL.

Any mention of EPA's 2017 recommended ECEL is conspicuously missing from the current draft risk evaluation. However, if EPA were to compare its workplace exposure estimates to the ECEL – as opposed to OSHA's PEL – a very different picture would emerge. For example, under the Manufacturing condition of use described above, the high-end 8-hr TWA Exposure Concentration (4.6 mg/m³ or 1.32 ppm) would just exceed the ECEL of 1.3 ppm. (Also see section 5.D. for discussion of EPA's decision to ignore relevant manufacturing exposure data.)

F. EPA did not rely on either an aggregate or sentinel exposure assessment.

"In conducting a risk evaluation ***, [EPA] shall—describe whether aggregate or sentinel exposures to a chemical substance under the conditions of use were considered, and the basis for that consideration." 15 U.S.C. § 2605(b)(4)(F)(ii). As explained below, EPA does not ultimately rely on either aggregate or sentinel exposures in its risk evaluation, and EPA has failed to explain how its decision to rely on other exposure assessments can be reconciled with TSCA § 6(b)(4)(F)(ii).

⁷⁹ Methylene Chloride and N-Methylpyrrolidone; Regulation of Certain Uses Under TSCA Section 6(a), 82 Fed. Reg. 7464, 7470 (proposed Jan. 19, 2017), <https://www.regulations.gov/docket?D=EPA-HQ-OPPT-2016-0231>.

⁸⁰ Letter from David Michaels, PhD, MPH, Assistant Secretary, U.S. Dep't of Labor, Occupational Safety & Health Admin., to James J. Jones, Assistant Administrator, U.S. EPA, Office of Chem. Safety & Pollution Prevention (Mar. 31, 2016), <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0231-0153>.

⁸¹ U.S. EPA, Recommendation for an Existing Chemical Exposure Concentration Limit (ECEL) for Occupational Use of Methylene Chloride and Workplace Air Monitoring Methods for Methylene Chloride [RIN 2070-AK07] (Nov. 2016), <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0231-0253>.

i. EPA did not perform an aggregate exposure assessment.

EPA's regulations define "[a]ggregate exposure [as] the combined exposures to an individual from a single chemical substance across multiple routes and across multiple pathways." 40 C.F.R. § 702.33. In the draft risk evaluation, EPA did not actually prepare an aggregate exposure assessment. (p. 387). EPA states that it considered exposure "to methylene [chloride via] inhalation and dermal contact separately." (p. 387). "EPA chose not to employ simply additivity of exposure pathways at this time within a condition of use because of the uncertainties present in the current exposure estimation procedures." (p. 387). "This lack of aggregation may lead to an underestimate of exposure, but based on physical chemical properties the majority of the exposure pathway is believed to be from inhalation exposures." (p. 387). Thus, EPA underestimates exposure and invokes uncertainty, without further explanation, as its excuse for that underestimation. Moreover, to the extent there are uncertainties in an "additivity" analysis, such uncertainties do not support assuming exposure is less than the sum of the exposures; by not combining the exposures it is far more likely that EPA is underestimating the exposure than overestimating it. Uncertainty does not justify ignoring the fact that these exposures are actually experienced in combination.

Notably, EPA did not merely fail to combine exposures between inhalation and dermal exposure pathways; EPA also failed to combine any exposures from multiple conditions of use. Instead, EPA looked at each condition of use separately, and EPA never considered the possibility that the same individual might be exposed to methylene chloride through multiple conditions of use. Thus, EPA failed to assess "the combined exposures to an individual from a single chemical substance across multiple routes and across multiple pathways." 40 C.F.R. § 702.33.

To accurately assess overall exposure to methylene chloride, EPA should prepare an exposure assessment that actually looks at "the combined exposures to an individual from a single chemical substance across multiple routes and across multiple pathways." 40 C.F.R. § 702.33. Such an exposure assessment should combine exposures from both the inhalation and dermal pathways, and EPA should also consider the scenarios where individuals are exposed via multiple conditions of use.

EPA has not justified its decision to forego an aggregate exposure assessment beyond invoking "uncertainty," which is not a justification for underestimating the overall exposure to methylene chloride.

- ii. *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.*

EPA’s regulations describe “[s]entinel exposure [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 C.F.R. § 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 gloves scenario within each [Occupational Exposure Scenario].” (p. 387). However, EPA did not establish that the exposures it analyzed represent the “plausible upper bound of exposure relative to all other exposures” within the relevant categories. This regulatory definition requires that, when EPA prepares a sentinel exposure assessment for workers, EPA must identify or evaluate the worker whose exposure represents the upper bound of exposure. 82 Fed. Reg. 33,726, 33,733 (July 20, 2017). EPA has not established that, for each category of exposure, it actually identified and evaluated the worker whose exposure represents the upper bound of exposure.

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 personal protective equipment (PPE) unless EPA can establish that PPE is *always* used for the particular condition of use. As discussed in section 1.B., EPA has 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 Occupational Exposure, e.g., pp. 115, 116).

Notably, it does not appear that EPA actually relied on even its own asserted sentinel exposures when preparing its risk characterizations. Instead, in the risk characterizations, EPA often assumed that workers would use PPE, which does not reflect “the plausible upper bound of exposure.” 40 C.F.R. § 702.33. So, it appears that EPA prepared a set of exposure assessments that EPA characterized as “sentinel exposure,” but EPA did not rely on those exposure assessments in preparing its risk characterizations.

* * * * *

Thus, EPA’s risk characterizations did not rely on either aggregate or sentinel exposure assessments. EPA has not explained how its approach is consistent with TSCA § 6(b)(4)(F)(ii). To accurately assess the total risk presented by methylene chloride, EPA needs to consider combined exposures, including those faced by the most exposed individuals. In EDF’s view, EPA should prepare an actual aggregate exposure assessment.

6. EPA inappropriately dismisses or downgrades epidemiological data.

A. EPA dismisses human epidemiological studies and disregards their well-accepted value in public health risk assessment

Throughout the history of EPA, human epidemiological studies have served as the “gold standard” for assessing population risks and guiding the Agency’s efforts to protect public health and the environment. Epidemiological studies provide information critical to understanding the causes of disease, factors influencing population susceptibility, and the actual levels of exposure at which health effects occur. Integration of evidence from epidemiological, *in vivo* and *in vitro* can reduce uncertainties associated with each study design and allows for stronger scientific conclusions about risks.⁸²

The value of epidemiological data for human health risk assessment has been stated and reinforced by EPA and others over many years. For example:

- EPA’s 2005 Guidelines for Carcinogen Risk Assessment⁸³
 - “Data from epidemiologic studies are generally preferred for characterizing human cancer hazard and risk.”⁸⁴
 - “Epidemiologic data are extremely valuable in risk assessment because they provide direct evidence on whether a substance is likely to produce cancer in humans, thereby avoiding issues such as: species-to-species inference, extrapolation to exposures relevant to people, effects of concomitant exposures due to lifestyles.”⁸⁵
- EPA’s 1991 Guidelines for Developmental Toxicity Risk Assessment⁸⁶
 - “Since the purpose of risk assessment is to make inferences about potential risks to human health, the most appropriate data to be used are those deriving from studies of humans.”

⁸² Kathleen C. Deener, et al., *Epidemiology: a foundation of environmental decision making*, 28 J. OF EXPOSURE SCIENCE & ENVTL. EPIDEMIOLOGY 515-21 (Sept. 2018), <https://www.ncbi.nlm.nih.gov/pubmed/30185947>.

⁸³ U.S. EPA, *Guidelines for Carcinogen Risk Assessment* (2005), <https://www.epa.gov/risk/guidelines-carcinogen-risk-assessment>.

⁸⁴ *Id.* at pp. 1-11.

⁸⁵ *Id.* at pp. 2-3.

⁸⁶ U.S. EPA, *Guidelines for Developmental Toxicity Risk Assessment* p. 1 (1991), <https://www.epa.gov/risk/guidelines-developmental-toxicity-risk-assessment>.

- ATSDR’s 2005 Public Health Assessment Guidance Manual (Update)⁸⁷
 - “Clearly, a study based on human data holds the greatest weight in describing relationships between a particular exposure and a human health effect. Fewer uncertainties exist about potential outcomes documented in well-designed epidemiologic studies.”
- Members of the risk assessment research community:⁸⁸
 - “Epidemiology is essential to our understanding of the role of environmental exposures in human disease. After all, it is only by studying the human population that we will understand the complex interactions of the environment, social factors, heredity, and behavior that determine individual and population health”

The methylene chloride draft risk evaluation continues a highly concerning pattern of lack of careful consideration by EPA of all data and a tendency to dismiss epidemiological evidence despite its inherent strengths.

On p. 264, EPA presents a series of bullet points that aim to broadly criticize the use of epidemiology in risk assessment. However, the arguments presented do not support EPA’s broad criticisms of the use of epidemiological evidence nor its treatment of specific studies.

The first of these arguments criticizes the use of the general population as an inappropriate referent group in the estimation of SMRs/SIRs due to the healthy worker effect. While the general population is not an ideal referent group in these estimations, the comparison is not without merit; effects observed under these circumstances likely underestimate risks to the general population resulting from the exclusion of more vulnerable persons from worker cohorts.

The second argument presents limitations in exposure information as an inherent flaw in epidemiological studies and discusses the potential for differential misclassification to over- or under-estimate effects. While misclassification is an important consideration in interpretation of epidemiological studies on a case-by-case basis, the potential for such a bias should not be presented as part of a broader rationale for dismissing epidemiological evidence.

The third argument suggests that restrictions on workplace smoking make worker populations less comparable to the general population, who does not experience such restrictions and (according to EPA) may have higher rates of smoking. As with our criticism of the first argument, such differences between the worker population and the general population likely have a dampening effect on any estimates of association. This dampening effect is not a

⁸⁷ ATSDR, Public Health Assessment Guidance Manual (Update) (Jan. 2005), https://www.atsdr.cdc.gov/hac/phamannual/pdfs/phagm_final1-27-05.pdf.

⁸⁸ Kieve E. Nachman, et al., *Leveraging epidemiology to improve risk assessment*, 4 OPEN EPIDEMIOLOGY J. 3-29 (2011), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6655421/>.

sufficient rationale for sweeping dismissal of the epidemiological evidence; instead, it is a consideration when weighing confidence in individual studies.

Taken together, EPA's attempt to summarize these criticisms and project them upon the broader body of human evidence is unhelpful and misleading. The agency should instead apply specific criticisms where applicable to its discussion of individual studies and focus its assessments of the weight of evidence on the strengths and limitations on the entire study database.

B. EPA's approach to and application of systematic review data quality criteria suggest bias and are inconsistent.

EPA applied its Office of Pollution Prevention and Toxics' (OPPT) updated data quality criteria to epidemiological studies in this draft risk evaluation. The completed data quality evaluation for these studies was provided in the Systematic Review Supplemental File.⁸⁹ We have identified several problems with EPA's approach to evaluating the epidemiological evidence, both with the employed tool and with the application of that tool and its effect on the disposition of the human evidence.

- i. OPPT provides neither explanation nor empirical support for its revisions to the systematic review data quality criteria for epidemiological studies, which make it difficult for epidemiological studies to be scored as overall as high quality.*

EPA OPPT provide neither an explanation nor empirical support for its revisions to the systematic review data quality criteria for epidemiological studies, and certain revisions make it more difficult for epidemiological studies to be scored overall as high quality. EPA OPPT's scoring methodology is already at odds with best practices in systematic review, see our earlier comments on OPPT's Application of Systematic Review in TSCA Risk Evaluations,⁹⁰ and the agency's decision to alter scoring criteria without providing any empirical rationale for the changes further underscores that the study quality evaluation strategy that OPPT developed is not evidence-based.

Further, at least six metrics in EPA OPPT's updated epidemiological criteria can no longer receive a score of High, including Metric 5 (Exposure Levels) and Metric 15 (Statistical Models). Since these individual metrics can at best be rated as Medium (a change from the earlier epidemiological criteria), epidemiological studies are thus less likely to be considered

⁸⁹ U.S. EPA, *Risk Evaluation for Methylene Chloride Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies – Epidemiological Studies CASRN: 75-09-2* (Oct. 2019), https://www.epa.gov/sites/production/files/2019-10/documents/10_draft_systematic_review_supplemental_file_data_quality_evaluation_of_human_health_hazard_studies_-_epidemiological_studies.pdf.

⁹⁰ EDF Comment on EPA's Systematic Review, <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2018-0210-0077>.

high quality overall and as a result may be given more limited consideration than other types of evidence (animal and *in vitro* studies), where it is remains possible to score High across every data quality metric.

In addition to issues with individual scoring criteria, the scheme used to calculate the overall rating for a particular study is not clearly presented in either the updated criteria document or the completed evaluation. The following equation is presented for calculating the overall rating:⁹¹

* MWF = Metric Weighting Factor

† High = 1; Medium = 2; Low = 3; Unacceptable = 4; N/A has no value.

‡ The overall rating is calculated as necessary. EPA may not always provide a comment for a metric that has been categorized as High.

$$\text{Overall rating} = \begin{cases} 4 & \text{if any metric is Unacceptable} \\ \left[\frac{\sum_i (\text{Metric Score}_i \times \text{MWF}_i)}{\sum_j \text{MWF}_j} \right]_{0.1} & \text{(round to the nearest tenth) otherwise} \end{cases}$$

where High $\Rightarrow \geq 1$ to < 1.7 ; Medium $\Rightarrow \geq 1.7$ to < 2.3 ; Low $\Rightarrow \geq 2.3$ to ≤ 3.0 . If the reviewer determines that the overall rating needs adjustment, the original rating is crossed out and an arrow points to the new rating.

The subscripts of i and j are not defined, and the final subscript of 0.1 is not explained. From this description, it is not possible to see how EPA OPPT calculated its overall ratings for these studies.

Given the concerns related to the appropriateness of the OPPT tool for epidemiological studies and the effect of its application in the context of methylene chloride, the agency should consider other study evaluation tools that are more appropriate for the consideration of the quality of observational epidemiologic studies. Examples include the Conducting Systematic Reviews and Meta-Analyses of Observational Studies of Etiology (COSMOS-E) tool (Dekkers, Vandenbroucke et al. 2019) and the Navigation Guide (Woodruff and Sutton 2014).

ii. EPA's application of the OPPT tool lacks a consistent framework: an illustrative example.

With regard to specific applications of the EPA OPPT tool, we also note that there are cases where 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

⁹¹ See, e.g., U.S. EPA, *Risk Evaluation for Methylene Chloride Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies – Epidemiological Studies* CASRN: 75-09-2 p. 5 (Oct. 2019), https://www.epa.gov/sites/production/files/2019-10/documents/10_draft_systematic_review_supplemental_file_data_quality_evaluation_of_human_health_hazard_studies_epidemiological_studies.pdf.

autism spectrum disorder for four epidemiological studies: Roberts et al. 2013,⁹² Talbott et al. 2015,⁹³ Windham et al. 2006,⁹⁴ Kalkbrenner et al. 2010.⁹⁵ NATA exposure estimates capture annual average concentrations, a potential limitation in understanding exposure estimate during critical windows of pregnancy. Among these studies that use NATA data, Roberts et al. (2013) and Kalkbrenner et al. (2010) received an overall “High” rating, while Talbott et al. (2015) and Windham et al. (2006) received borderline “Medium” ratings overall.

The agency notes that a single study used average monthly methylene chloride measurements from monitoring stations in Los Angeles County to estimate exposure among pregnant women during the perinatal period.⁹⁶ This study did not find a significant association between methylene chloride exposure and autism risk, in contrast with the studies using NATA data. Even though exposure estimates from studies using NATA data are less preferable (because they are modeled and not directly measured), the use of such data is subject to non-differential exposure misclassification, which likely biases measured associations towards the null. Further, when taken together, these four studies represent multiple epidemiological cohorts and cover a more comprehensive geography (multiple states) than the von Ehrenstein study (which only looked at a single county in California).

In spite of the body of evidence, EPA elected not to advance the ASD endpoint fully on the basis of the von Ehrenstein study, and chose to dismiss the findings of the other four studies without discussing their merits and considering the weight of the evidence across studies that employ different exposure estimation methodologies. EPA should develop a framework for weighing evidence when multiple studies using different methodologies yield different results. In this specific instance, 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.

⁹² Andrea L. Roberts, et al., *Perinatal air pollutant exposures and autism spectrum disorder in the children of Nurses' Health Study II participants*, 121:8 ENVTL. HEALTH PERSPECTIVES 978-84 (Aug. 2013), <https://www.ncbi.nlm.nih.gov/pubmed/23816781>.

⁹³ Evelyn O. Talbott, et al., *Air toxics and the risk of autism spectrum disorder: the results of a population based case-control study in southwestern Pennsylvania*, 14 ENVTL. HEALTH (Oct. 2015), <https://www.ncbi.nlm.nih.gov/pubmed/26444407>.

⁹⁴ Gayle C. Windham, et al., *Autism Spectrum Disorders in Relation to Distribution of Hazardous Air Pollutants in the San Francisco Bay Area*, 114:9 ENVTL. HEALTH PERSPECTIVES 1438-44 (Sept. 2006), <https://www.ncbi.nlm.nih.gov/pubmed/16966102>.

⁹⁵ Amy Kalkbrenner, et al., *Perinatal Exposure to Hazardous Air Pollutants and Autism Spectrum Disorders at Age 8*, 21:5 EPIDEMIOLOGY 631-41 (Sept. 2010), <https://www.ncbi.nlm.nih.gov/pubmed/20562626>.

⁹⁶ Ondine von Ehrenstein, et al., *In Utero Exposure to Toxic Air Pollutants and Risk of Childhood Autism*, 25:6 EPIDEMIOLOGY 851-58 (Nov. 2014), <https://www.ncbi.nlm.nih.gov/pubmed/25051312>.

7. EPA's environmental assessment raises a number of questions and concerns.

A. EPA cannot ignore environmental releases of a chemical because it cannot attribute each release to a particular condition of use.

EPA has indicated that “only a few USGS-NWIS and STORET monitoring stations aligned with the watersheds of the methylene chloride-releasing facilities *identified under the scope* of this assessment, and the co-located monitoring stations had samples with concentrations below the detection limit; therefore, *no direct correlation* can be made between them.” (p. 370, emphases added). This language suggests EPA may believe it must be able to attribute every environmental release of a chemical to a particular condition of use or facility in order to consider its risks in a risk evaluation. This is not the case.

EPA must conduct risk evaluations under TSCA that consider all “reasonably available” information relating to a chemical substance, including information that may not be tied to specific conditions of use. 15 U.S.C. § 2625(k). EPA's rules further define “reasonably available information” as “information that EPA possesses or can reasonably generate, obtain and synthesize for use ***.” 40 C.F.R. §§ 702.3, 702.33.

Based on its statement in the draft risk evaluation cited above and on public comments made recently by EPA staff members, EPA appears to be arguing that it cannot use certain data sources because the data cannot be attributed back to a particular source or condition of use. This rationale provides no basis for ignoring these data. Nothing in TSCA allows EPA to ignore data simply because they have not been tied to a particular condition of use, let alone a particular facility. To the contrary, TSCA instructs EPA to consider *all* reasonably available information, which is in direct conflict with what EPA has done here.

Data that cannot be attributed to specific conditions of use are still relevant to determining whether *the chemical substance* presents an unreasonable risk, and as such must be considered by EPA. EPA cannot ignore data simply because it has not determined or even cannot determine how much of the exposure is attributable to a particular condition of use. Such a consideration may be more relevant at any subsequent risk management stage, when EPA may need to understand the extent to which specific measures will reduce exposure and risk. But that future need provides no basis for EPA to ignore risk-relevant information at the risk evaluation stage.

B. EPA has failed to adequately address risks to terrestrial organisms.

EPA ignores important pathways of methylene chloride exposure to terrestrial organisms based on unclear and apparently non-conservative assumptions.

In its problem formulation, EPA initially stated: “Terrestrial species populations living near industrial and commercial facilities using methylene chloride may be exposed via multiple routes such as ingestion of surface waters and inhalation of outdoor air.” (p. 37). EPA then seeks to justify not analyzing exposure to terrestrial organisms through water, sediment, or migration from biosolids via soil deposition, based on an assertion that “[t]errestrial species exposures to MC [methylene chloride] in water are orders of magnitude below hazardous concentrations.” (Problem Formulation, Appendix E, pp. 139-140)⁹⁷ It is far from clear from the Problem Formulation how EPA managed to conclude that methylene chloride is present in water only at levels that are orders of magnitude below concentrations of concern.

In its draft risk evaluation, EPA states: “A screening of hazard data for terrestrial organisms shows potential hazard; however, physical chemical properties do not support an exposure pathway through water and soil pathways to terrestrial organisms.” (p. 299) EPA did not bother to calculate acute and chronic concentrations of concern (COC) for terrestrial organisms in its problem formulation, as it had done in its other problem formulations for other chemicals. EPA explicitly states that it has not applied adjustment factors to the hazard levels listed on pp. 43-44 of the problem formulation:

It should be noted that these hazard levels of concern do not account for differences in inter- and intra-species variability, as well as laboratory-to-field variability and are dependent upon the availability of datasets that can be used to characterize relative sensitivities across multiple species within a given taxa or species group, since the data available for most industrial chemicals are limited.
(p. 44)

EPA typically applies a 5x adjustment factor for acute toxicity and 10x for chronic toxicity for ecological receptors to account for such variability, and has done so in other problem formulations.

While EPA provides several hazard values based on acute exposure, mostly limited to lethality (as opposed to other organism- or population-level effects), EPA has not found or provided any chronic toxicity data for terrestrial organisms other than a NOAEC (only for inhalation, based on concentration in air) for mammals. There are no oral toxicity data for terrestrial organisms (other than laboratory rodents) – a data gap that EPA fails to acknowledge.

Furthermore, despite recognizing methylene chloride’s high volatility, high vapor density, and long-range transport in air (p. 64)—all factors which increase potential air exposures to terrestrial organisms—EPA has completely ignored inhalation exposures to terrestrial species, stating:

⁹⁷ EPA also excludes exposure to terrestrial organisms from the ambient air pathway based on the unsupported argument that such exposures are adequately managed by the Clean Air Act (see section 2.B.).

EPA did not include the emission pathways to ambient air from commercial and industrial stationary sources or associated inhalation exposure of terrestrial species, because stationary source releases of methylene chloride to ambient air are adequately assessed and any risks effectively managed under the jurisdiction of the Clean Air Act (CAA). (p. 299)

However, in addition to the fact that several million pounds of methylene chloride are released annually into the air (see section 2.B of these comments), 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 disproportionately impacted by methylene chloride. In its literature review, EPA dismissed a study that not only identified a bioconcentration factor (BCF) of 577 in water moss (Thiebaud et al. 1994),⁹⁸ but also states that concentrations at the water-atmosphere interface may be more significant than aquatic concentrations.

Thiebaud et al. (1994) used radiolabeled methylene chloride to understand its fate at sublethal concentrations (approximately 4 ppb) in aquatic environments. The authors noted that water moss (*F. antipyretica*) had the highest accumulation factor of 577, though it also had high variability across the three replicates. Duckweed (*Lemna minor*), which resides at the water-atmospheric interface, consistently accumulated the most methylene chloride of the species tested (largest accumulation factor of 112). The authors hypothesize that its interface location, where "the concentration of these volatile organic compounds were greater than in depth" leads to accumulation via active or passive adsorption. It should be noted that EPA's modeled surface water concentrations of methylene chloride ranged as high as 17,000 ppb. Not only are these concentrations well above the COC for aquatic organisms (see section 7.C. of these comments), these model results suggest another potential route of exposure to methylene chloride through its volatilization.

EPA unjustifiably disregarded this study. According to the Systematic Review Supplemental File: Data Quality Evaluation of Environmental Hazard Studies,⁹⁹ EPA determined the study to be of unacceptable quality, despite giving it a mean score of 1.5 (defined as "High" quality) due

⁹⁸ H. Thiebaud, et al., *Fate of a volatile chlorinated solvent in indoor aquatic microcosms: sublethal and static exposure to [¹⁴C]dichloromethane*, 28:1 ECOTOXICOLOGY & ENVTL. SAFETY 71-81 (June 1994),

<https://www.sciencedirect.com/science/article/abs/pii/S0147651384710359?via%3Dihub>.

⁹⁹ U.S. EPA, *Risk Evaluation for Methylene Chloride Systematic Review Supplemental File: Data Quality Evaluation of Environmental Hazard Studies* CASRN: 75-09-2 pp. 63-64 (Oct. 2019), https://www.epa.gov/sites/production/files/2019-10/documents/8_draftsystematic_review_supplemental_file_data_quality_evaluation_of_environmental_hazard_studies.pdf.

to one metric EPA found to be unacceptable. Specifically, 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 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. Not only does this study examine accumulation factors, it also indicates that the volatility of methylene chloride may contribute to potential impacts to ecosystems through air exposure subsequent to discharges to water.

EPA needs to provide a rational and clear analysis based on the best available science and reasonably available information to support its conclusions, and at this point, it has failed to do so.

C. EPA’s analysis of aquatic risks may underestimate the risk.

As explained more in section 9.B., EPA’s own analyses showed that methylene chloride presents an unreasonable risk to aquatic organisms. (pp. 389, 286-87). Specifically, EPA found that releases from certain disposal and recycling facilities would result in surface water concentrations well above the concentration of concern (COC) for methylene chloride. (pp. 427-28). But if anything, EPA’s analysis may have underestimated the total risk from these releases.

For example, when estimating the releases from one facility where the surface water concentration exceeded the concentration of concern, 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.

In addition, for those facilities where modeled surface water concentrations exceed the chronic concentration of concern, three of the facilities engaged in transfers to the same facility—Clean Harbors Baltimore (p. 287). EPA did not address why these releases should not be considered together and combined to result in an even higher surface water concentration of methylene chloride than when considered separately. Particularly given that the modeled results for each of the three facilities indicate a risk, analyzed separately, EPA should have considered how they may combine to present an even greater risk.

8. EPA's draft risk evaluation suffers from major data gaps and associated analytical inadequacies.

A. EPA needs to apply an uncertainty factor (UF) to account for lack of dermal toxicity data.

The draft risk evaluation states that “No acceptable toxicological data are available by the dermal route” (p. 217) and that “EPA did not identify toxicity studies by the dermal route that were adequate for dose-response assessment. Dermal candidate values, therefore, were derived by route-to-route extrapolation from the inhalation PODs as mentioned above” (p. 282). As EDF has commented on for prior draft risk evaluations that take a similar approach, 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,^{100,101} EPA should apply an additional uncertainty factor of 10 to account for these uncertainties.

B. EPA has made inappropriate assumptions about activity rates in its route-to-route extrapolation for dermal PODs.

In extrapolating from inhalation PODs to the dermal route, EPA assumes a “ventilation rate of 1.25 m³/hr (for light activity)” (p. 282). The rationale for this parameter is that “EPA assumes that activities involving methylene chloride exposure involve some movement, and thus, assumes a ventilation rate for light activity” (p. 282). However, given the range of potential activities involving movement when utilizing methylene chloride across different conditions of use, it is quite possible if not likely that individuals could exceed “light activity” as described by EPA. As such, it is inappropriate for the Agency to provide such sweeping assumptions without adequate supporting evidence.

Acknowledging the potential for higher activity patterns (and the associated increases in ventilation) is important, since EPA acknowledges that “[i]t has been shown that greater metabolism to CO occurs in individuals who are exercising (Nac/Aegl, 2008)” (p. 274).

By assuming only “light activity” in this draft risk evaluation, EPA ignores the potential elevated risk faced by high-activity individuals. If data on activity patterns in occupational or consumer

¹⁰⁰ See, e.g., Schröder, K., et al., *Evaluation of route-to-route extrapolation factors based on assessment of repeated dose toxicity studies compiled in the database RepDose®*, 261 TOXICOLOGY LETTERS 32-40 (Nov. 2016), <https://www.ncbi.nlm.nih.gov/pubmed/27553675>; Dankovic, D.A., et al., *The scientific basis of uncertainty factors used in setting occupational exposure limits*, 12 J. OF OCCUPATIONAL & ENVTL. HYGIENE 55-68 (Nov. 2015), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4643360/>.

¹⁰¹ Rennen, MA, et al., *Oral-to-inhalation route extrapolation in occupational health risk assessment: a critical assessment*, 39:1 REG. TOXICOLOGY & PHARMACOLOGY 5-11 (2004), <https://www.ncbi.nlm.nih.gov/pubmed/14746775>.

users are not available, then, at minimum, EPA should conduct sensitivity analyses incorporating various ventilation rates corresponding to different activity patterns.

C. EPA lacks crucial developmental neurotoxicity data.

Despite 1) the well-recognized CNS effects of methylene chloride (e.g. Sections 3.2.3.1.1 and 3.2.3.1.4) and 2) identification of fetuses as a sensitive population (pp. 32, 274), the lack of data on potential developmental neurotoxicity is highly concerning. The only passing mention of this subject is on p. 223 of the draft risk evaluation, where EPA states that:

Bornschein et al. (1980), reported increased general activity and delayed rates of habituation to a novel environment in rats exposed to 4500 ppm before (about 21 days) and/or during gestation (to day 17). Neurological endpoints have not been measured in other animal reproductive or developmental studies of methylene chloride.

However, in the 2011 IRIS assessment, the Agency highlighted that “[t]he relatively high activity of CYP2E1 in the brain compared to the liver of the developing human fetus raises the potential for neurodevelopmental effects from dichloromethane exposure.”¹⁰² The IRIS program then explicitly acknowledges this data gap:

The potential for gestational exposure to CO and to dichloromethane (through its transfer across the placenta) resulting from maternal dichloromethane exposure via oral and inhalation routes raises concerns regarding neurodevelopmental effects.... [T]here are no studies that have adequately evaluated neurobehavioral and neurochemical changes resulting from gestational dichloromethane exposure.... The potential for developmental neurotoxicity occurring at lower exposures to dichloromethane represents a data gap.¹⁰³

To adequately protect this sensitive subpopulation, EPA must act immediately to fill this data gap. In the interim, EPA must explicitly acknowledge this gap and include an additional database UF for its non-cancer risk estimates. As summarized in EPA’s *Review of the Reference Dose and Reference Concentration Processes Document*, the “database UF is intended to account for the potential for deriving an underprotective RfD/RfC as a result of an incomplete characterization of the chemical’s toxicity.”¹⁰⁴ This additional UF is utilized when “data are

¹⁰² U.S. EPA, *Toxicological Review of Dichloromethane (Methylene Chloride)* p. 165 (2011), https://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/0070tr.pdf.

¹⁰³ *Id.* at p. 92.

¹⁰⁴ U.S. EPA Risk Assessment Forum, *A Review of the Reference Dose and Reference Concentration Processes* p. 4-44 (Dec. 2002), <https://www.epa.gov/sites/production/files/2014-12/documents/rfd-final.pdf>.

unavailable or are insufficient to explicitly consider the potential sensitivity of the developing organism.”¹⁰⁵

9. EPA’s unreasonable risk definition and risk determinations are severely flawed.

A. EPA grossly underestimates occupational risk, leading to ‘no unreasonable risk’ findings or understatements of the extent and magnitude of the unreasonable risks it does find.

EPA underestimates occupational risks in five major ways in its draft risk evaluation:

1. EPA assumes that workers will wear fully effective personal protective equipment (respirators and gloves) in many scenarios and relies on that assumption to avoid finding unreasonable risk or understate the extent and magnitude of the risk. See sections 5.A. and 5.B. and subsection i. below for the details.
2. EPA finds a cancer risk to workers unreasonable only if it exceeds a level of 1 in 10,000 – which is as much as 100 times higher a risk than warrants regulation under TSCA to protect workers and other vulnerable subpopulations. See subsection ii. below for the details.
3. For ONUs EPA has failed to identify unreasonable risks for the most highly exposed, and hence most vulnerable, unless it finds that the majority of ONUs also face unreasonable risks. See subsection iii. below for the details.
4. For dermal exposures, EPA negates unreasonable risk findings when they are “close” to a risk benchmark. See subsection iv. below for the details.
5. EPA has dismissed numerous unreasonable risk findings by invoking “uncertainty” or unwarranted use of PPE, or without any explanation at all. See subsection v. below for the details.

The effect of each of these decisions is to underestimate occupational risk– ultimately either leading EPA to determine “no unreasonable risk” or to grossly understate the extent and magnitude of the unreasonable risks it does find. Below we discuss each of these issues in further detail.

- i. By assuming use of PPE, EPA conflates risk evaluation and risk management and significantly understates risk.*

TSCA intentionally divides risk evaluation and risk management into two distinct processes, whereby regulatory measures are to be considered *after* EPA finds an unreasonable risk. However, by choosing to make risk determinations based on an assumption of PPE, EPA conflates risk evaluation and risk management and leads EPA either not to find unreasonable risk

¹⁰⁵ *Id.* at p. 4-40.

or to underestimate the extent and magnitude of that risk in a number of scenarios – thereby denying itself the authority to impose mandatory requirements sufficient to control workplace exposures (see sections 5.A. and 5.B.).

For example, Table 4-70 (p. 346-347) demonstrates that for non-cancer risk from chronic dermal exposure, EPA has actually found excessive risk in the absence of glove use in *every* occupational scenario it examined. Even assuming gloves with a PF of 5, EPA found excessive risk under every high-end exposure scenario. Yet, when it comes to the risk determinations, EPA makes no unreasonable risk determinations based on dermal exposure, invoking PPE (p. 428). EPA's failure to make an unreasonable risk determination based on dermal exposure could constrain its authority to require that the gloves it assumed are used will actually be used.

See EDF's further critique of EPA's assumption of PPE use in the workplace in sections 1.B., 5.A., and 5.B.

ii. EPA's use of a 1 in 10,000 cancer risk level as reasonable for workers is deeply flawed.

a. EPA's approach must be rejected on scientific as well as legal grounds.

EPA has proposed to establish 1×10^{-4} as the cancer risk benchmark for workers (pp. 425, 426). EPA cites NIOSH guidance and the *Benzene* decision for support (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. EPA's decision is wholly at odds with its own acknowledgment two pages earlier that other laws have standards that differ from TSCA's (p. 424, footnote 21).

EPA is required to protect workers, both generally and as a "potentially exposed or susceptible subpopulation," under TSCA, not under OSHA. 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.

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 1×10^{-4} benchmark (p. 426, footnote 22).

Indeed, EPA's reliance on the *Benzene* decision cannot be reconciled with the statutory differences between OSHA's standard and TSCA's unreasonable risk standard. In the *Benzene*

case, the Court interpreted a provision of the OSH Act that defined standards as “reasonably necessary or appropriate to provide safe or healthful employment and places of employment,” as requiring OSHA “to make a threshold finding that a place of employment is unsafe—in the sense that *significant* risks are present and can be eliminated or lessened by a change in practices.” *Indus. Union Dep’t, AFL-CIO v. API*, 448 U.S. 607, 642 (D.C. Cir. 1980) (emphasis added). The Court’s interpretation turned on the statutory language of the OSH Act, the Act’s structure, and its legislative history. But EPA can point to *no* statutory language in TSCA invoking this standard, EPA has pointed to no similarities between the two statute’s structures, nor has EPA pointed to any legislative history suggesting that TSCA adopted the OSH Act’s standard. Moreover, if Congress had intended to adopt the *Benzene* standard under TSCA, it would have required that EPA regulate “significant risks,” not “unreasonable risks.” Indeed, the significant differences between the language and structure of the two statutes strongly indicates that Congress meant to adopt a different standard in TSCA, not the standard articulated by the Court in the *Benzene* case.

Moreover, in implementing TSCA (even before the amendments) and its other environmental statutes, EPA has generally sought to reduce population risks from chemicals in commerce that are carcinogens to below about one case per one million people. See, for example, this EPA statement from 1989: “EPA believes *** that it should reduce risks to less than 1×10^{-6} for as many exposed people as reasonably possible.” National Emission Standards for Hazardous Air Pollutants; Radionuclides, 54 Fed. Reg. 51,654, 51,686 (Dec. 15, 1989). Nor does EPA only apply this standard under the Clean Air Act. When setting Clean Water Act criteria, “EPA intends to use the 10^{-6} risk level, which the Agency believes reflects an appropriate risk for the general population. EPA’s program office guidance and regulatory actions have evolved in recent years to target a 10^{-6} risk level as an appropriate risk for the general population. EPA has recently reviewed the policies and regulatory language of other Agency mandates (e.g., the Clean Air Act Amendments of 1990, the Food Quality Protection Act) and believes the target of a 10^{-6} risk level is consistent with Agency-wide practice.”¹⁰⁶ When Congress amended TSCA to include the unreasonable risk standard, it did so knowing that agency practice was to regulate cancer risks at the 10^{-6} risk level. It should be presumed that Congress meant to adopt this risk standard when codifying the unreasonable risk standard.

In grasping for support for its approach in this risk evaluation by citing other mentions by EPA of the 1×10^{-4} risk level (p. 426, footnote 22), EPA blurs a critical distinction made when EPA has invoked the less stringent level of protection from cancer risks: the level set to reflect the maximum risk faced by any individual vs. the level set to protect a broader population. EPA invokes the “two-step approach” used under the Clean Air Act, where EPA includes a “limit on

¹⁰⁶ U.S. EPA, *Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health* p. 2-6 (2000), <https://www.epa.gov/sites/production/files/2018-10/documents/methodology-wqc-protection-hh-2000.pdf>.

maximum individual lifetime [cancer] risk (MIR) of approximately 1 in 10 thousand” (p. 426 n. 22, citing 54 Fed. Reg. 38,045 (Sept. 14, 1989)) (emphasis added). But that is entirely different than the level set to protect the vast majority of the population in question.

More specifically, the two-step, risk-based decision framework for the National Emission Standard for Hazardous Air Pollutants (NESHAP) program is described as follows by EPA:

First, the rule sets an upper limit of acceptable risk at about a 1-in-10,000 (or 100-in-1 million) lifetime cancer risk for the *most exposed person*. As the rule explains, “The EPA will generally presume that if the risk to that individual [the Maximum Individual Risk] is no higher than approximately 1 in 10 thousand, that risk level is considered acceptable and EPA then considers the other health and risk factors to complete an overall judgment on acceptability.”

Second, the benzene rule set a target of protecting the *most people possible* to an individual lifetime risk level no higher than about *1-in-1 million*.¹⁰⁷

But 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 methylene chloride 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.

b. EPA’s approach leads to a massive understatement of the extent to which workers and ONUs face unreasonable risk from methylene chloride exposure.

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, EDF examined EPA’s cancer risk estimates for each of its 65 conditions of use (COUs) involving inhalation exposures to workers and ONUs and each of its 23 occupational exposure scenarios (OES) involving potential dermal exposures to workers. EPA’s estimates are presented in the tables in Section 4.2.2.1 (for inhalation) and Section 4.2.2.2 (for dermal exposure) in the draft risk evaluation.

While EPA applied a 10^{-4} cancer risk benchmark to these estimates, EDF looked at whether they exceed a cancer risk benchmark of 10^{-5} or 10^{-6} and should have at least potentially been identified as presenting an unreasonable risk to workers.

¹⁰⁷ WHAT DOES EPA BELIEVE CONSTITUTES AN ACCEPTABLE LEVEL OF RISK?, <https://www.epa.gov/national-air-toxics-assessment/nata-frequent-questions#risk2> (emphasis added) (last visited Nov. 26, 2019).

The details of EDF's analysis are provided in the spreadsheet EDF submitted along with these comments.¹⁰⁸ We summarize the results below, first for inhalation exposures and then form dermal exposures.

Inhalation cancer risk

For cancer risks from inhalation, across the various COUs EPA considered the following cases:

- Workers, high-end exposure, no PPE assumed
- Workers, high-end exposure, PPE assumed
- Workers, central tendency exposure, no PPE assumed
- Workers, central tendency exposure, PPE assumed
- ONUs, high-end exposure, no PPE assumed
- ONUs, central tendency exposure, no PPE assumed

Across these six cases for the 65 COUs, EPA's cancer risk benchmark of 10^{-4} was exceeded **88 times**. Our analysis found that, relative to EPA's 10^{-4} cancer risk benchmark:

- a 10^{-5} cancer risk benchmark was exceeded *an additional* **146 times, for a total of 234 exceedances**; and
- a 10^{-6} cancer risk benchmark was exceeded *an additional* **214 times, for a total of 302 exceedances**.

The breakdown for each of the six cases is presented in the table below.

¹⁰⁸ See Appendix B.

**Table C: Number of Cancer Risk Estimates Exceeding
EPA's and Other More Appropriate Cancer Risk Benchmarks**

			Risk estimates exceeding a benchmark of 10⁻⁴	<i>Additional risk estimates exceeding a benchmark of 10⁻⁵</i>	<i>Additional risk estimates exceeding a benchmark of 10⁻⁶</i>
Worker	High end	No PPE	35	24	29
		PPE	1	25	32
	Central	No PPE	8	43	51
		PPE	1	5	31
ONU	High end	No PPE	35	15	29
	Central	No PPE	8	34	42
TOTAL for all 6 cases			88	146	214
GRAND TOTAL			88	234	302

Dermal cancer risk

Using its 10⁻⁴ cancer risk benchmark, EPA concluded that none of the 23 OESs presented unreasonable risk to workers¹⁰⁹ from cancer, from either high-end or central tendency exposures.

Our analysis found that:

- Using a 10⁻⁵ cancer risk benchmark:
 - Risks from high-end exposures exceeded the benchmark for 8 OESs.
 - Risks from central tendency exposures exceeded the benchmark for no OESs.
- Using a 10⁻⁶ cancer risk benchmark, risks from the high-end and central tendency exposures exceeded the benchmark for all 23 OESs.

This analysis shows that EPA's draft risk evaluation has dramatically understated the occupational cancer risks of methylene chloride.

iii. In nearly a third of its risk determinations, EPA inappropriately fails to find unreasonable risk despite exceedances of its benchmarks for high-end exposures.

In its draft risk evaluation for 1,4-dioxane, EPA unjustifiably decided 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. EPA has applied this flawed approach again here. EPA must ensure that it does not do so in the final risk evaluation.

¹⁰⁹ EPA assumed ONUs would not be dermally exposed under any scenario.

EPA states: “To account for those instances where monitoring data or modeling did not distinguish between worker and ONU inhalation exposure estimates, EPA considered the central tendency risk estimate when determining ONU risk” (p. 428). EPA also states (p. 431):

ONU inhalation exposures are expected to be lower than inhalation exposures for workers directly handling the chemical substance. To account for this uncertainty, EPA considered the central tendency estimate when determining ONU risk.

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 COUs¹¹⁰; for examples, see pp. 431, 436, 449.

Among other concerns, EPA’s approach is at odds with its obligation under TSCA to conduct risk evaluations that ensure protection of “potentially exposed or susceptible subpopulations,”

¹¹⁰ These COUs are:

- Manufacturing
- Import
- Processing as a reactant:
 - Intermediate in industrial gas manufacturing (e.g., manufacture of fluorinated gases used as refrigerants)
 - Intermediate for pesticide, fertilizer, and other agricultural chemical manufacturing
 - Petrochemical manufacturing
 - Intermediate for other chemicals
- Processing, adhesives and sealants:
 - Single component glues and adhesives and sealants and caulks (spray)
 - Single component glues and adhesives and sealants and caulks (non-spray)
- Metal products not covered elsewhere: Degreasers - non-aerosol (commercial/industrial)
- Automotive care products: Functional fluids for air conditioners: refrigerant, treatment, leak sealer
- Laundry and dishwashing products: Spot remover for apparel and textiles
- Lubricants and grease:
 - Liquid lubricants and greases
 - Non-aerosol degreasers and cleaners
- Other industrial and commercial uses:
 - Laboratory chemicals - all other chemical product and preparation manufacturing
 - Electrical equipment, appliance, and component manufacturing
 - Oil and gas drilling, extraction, and support activities
 - Toys, playground, and sporting equipment - including novelty articles (toys, gifts, etc.)
 - Carbon remover: brush cleaner, use in taxidermy, and wood floor cleaner
 - Carbon remover: lithographic printing cleaner

which TSCA explicitly defines as including workers. EPA represents its high-end estimates as “generally intended to cover individuals or sub-populations with greater exposure,” while its 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.

Moreover, EPA stated that it considered sentinel exposures, which it defines 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” (p. 387). 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 C.F.R. § 702.33.

iv. EPA shifts the goalposts when risk values are only a little below – but not above – its benchmark MOEs.

In this risk evaluation EPA has re-instituted a flawed approach it used for 1,4-dioxane, but did not rely on for 1-bromopropane, under which it can still deem a risk to be reasonable even though it exceeds the applicable acceptable level, as long as it is “close” to the acceptable level. Specifically, EPA states that it can ignore an unreasonable risk where “the risks are very nearly at the benchmarks (i.e. MOE of 9 for benchmark MOE of 10)” (p. 394). Indeed, EPA has applied this flawed approach to seven conditions of use where its dermal chronic non-cancer risk estimates, under its assumption that gloves with a protection factor (PF) of 10 will be used, result in a MOE below its benchmark MOE (Table 4-70, pp. 346-347).

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. See, for example, other entries in Table 4-70, PF=5 column, for Commercial Aerosol Product Uses, Paint and Coating Removers, Miscellaneous Commercial Non-Aerosol Use, and Laboratory Use (all Central Tendency): Here, a calculated MOE of 13 vs. the benchmark MOE of 10 is deemed not to represent unreasonable risk.

EPA’s approach to unreasonable risk violates its duties under TSCA. TSCA § 6 requires that EPA “shall conduct risk evaluations pursuant to this paragraph to determine whether a chemical substance presents an unreasonable risk of injury to health or the environment.” 15 U.S.C.

§ 2605(b)(4)(A). Here, EPA’s analysis of certain conditions of use finds an unreasonable risk with the estimated MOEs falling below the benchmark MOE, and EPA then reverses that finding because the estimated MOEs are “very nearly at the benchmarks.” By doing so, EPA adopts a finding on unreasonable risk that runs counter to the evidence before the agency. EPA’s own analysis establishes that a risk exists, and EPA has not explained how the MOEs being in “very nearly at the benchmarks” negates the finding of unreasonable risk. While EPA emphasizes that some uncertainties might overestimate the risk presented by these conditions of use, EPA fails to account for how these or other uncertainties might underestimate the risk. EPA’s failure to adopt a final risk determination consistent with its factual findings is arbitrary and capricious.

v. *EPA has dismissed numerous unreasonable risk findings by invoking “uncertainty” or without any explanation at all.*

a. *Dismissal of unreasonable risk based on “uncertainty”*

For at least three of its 65 COUs, EPA has merely invoked “uncertainty” in its information as a basis for dismissing an unreasonable risk.¹¹¹ These COUs are Import, Repackaging, and Plastic and rubber products (plastic manufacturing) (see pp. 432, 436, and 467). For example, on p. 436 for Repackaging, EPA states: “In consideration of the uncertainties in the exposures for ONUs for this COU, EPA has determined the non-cancer risks presented by chronic inhalation are not unreasonable.”

EPA’s own analyses in these cases showed that methylene chloride presents an unreasonable risk, but EPA dismisses this unreasonable risk by invoking uncertainty in the data. 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 is presented by these conditions of use.

Moreover, to the extent there are uncertainties in EPA’s analysis, such uncertainties counsel in favor of a finding of unreasonable risk – EPA could as easily be underestimating the risk presented by these conditions of use as overestimating them. Uncertainty increases the chances of an unreasonable risk; it does not diminish them. Uncertainty, standing alone, does not justify a finding of no unreasonable risk when EPA’s own analyses support a finding of unreasonable risk.

¹¹¹ These COUs are in addition to five others where EPA invokes uncertainty as a basis for relying solely on central tendency exposures, as previously discussed in section 9.A.iii.

b. Dismissal of unreasonable risk by invoking unwarranted use of PPE or without any explanation

For eight of its 65 COUs, EPA dismissed an unreasonable risk to workers by invoking PPE that the agency had already stated is not expected to be used.¹¹² 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. See, for example, Metal products not covered elsewhere: Degreasers - non-aerosol (commercial/industrial) (p. 449); and Automotive care products: Functional fluids for air conditioners: refrigerant, treatment, leak sealer (p. 451). However, as noted on those same pages, these are COUs for which "EPA does not expect routine use of respiratory PPE."

In two other cases, EPA dismisses an unreasonable risk with no explanation:

- In the case of Solvents (which become part of product formulation or mixture): All other chemical product and preparation manufacturing (pp. 460-461), EPA dismisses a cancer risk to ONUs without providing any explanation. This cannot be justified by assumed use of PPE, as ONUs are not expected by EPA to use PPE.
- In the case of Carbon remover: lithographic printing cleaner (pp. 473-474), EPA dismisses a cancer risk to workers with no explanation given. This cannot be justified by assumed use of PPE, as EPA stated that it does not expect PPE to be used.

All 10 of these cases entail approaches that are 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 workers or ONUs presented by these conditions of use.

¹¹² These COUs are for the following industrial and commercial uses:

- Metal products not covered elsewhere: Degreasers - non-aerosol (commercial/industrial)
- Automotive care products: Functional fluids for air conditioners: refrigerant, treatment, leak sealer
- Lubricants and grease:
 - Liquid lubricants and greases
 - Non-aerosol degreasers and cleaners
- Other uses:
 - Electrical equipment, appliance, and component manufacturing
 - Oil and gas drilling, extraction, and support activities
 - Toys, playground, and sporting equipment - including novelty articles (toys, gifts, etc.)
 - Carbon remover: brush cleaner, use in taxidermy, and wood floor cleaner

B. EPA cannot reasonably dismiss its findings of environmental risk merely by invoking uncertainty.

For environmental risk, EPA's own analyses showed that methylene chloride 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). Beyond this bald assertion, EPA provides no basis for its dismissal of identified risks anywhere in its draft risk evaluation.

EPA used a Risk Quotient (RQ) to compare environmental concentration to the effect level to characterize the risk to aquatic organisms. (p. 29). Under this approach, "[i]f the RQ is greater than 1, the exposure is greater than the effect concentration and there is potential for risk presumed." (p. 427). Based on EPA's own analyses, EPA found risks to aquatic organisms from four disposal and recycling facilities as well as one waste water treatment plant (WWTP), with the RQ exceeding 1 (in one case by nearly 200) (p. 287), but EPA dismissed this risk merely by invoking uncertainty. 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.

In summarizing its risk conclusions, EPA states that: "Risks to aquatic organisms were identified near four recycling and disposal facilities and one WWTP." (p. 389). But EPA then does not make risk findings. Instead, in the risk characterization section, EPA states that:

All but two conditions of use (recycling and disposal) had RQs < 1, indicating no unreasonable risk. *** However, there are specific facilities where estimate releases result in modeled surface water concentrations that exceed the aquatic benchmark. Given the uncertainties in the data for the limited number of data points above the RQ, EPA does not consider these risks unreasonable (see Section 4.1.2). (p. 428)

EPA essentially acknowledges that it did find unreasonable risk for recycling and disposal, and EPA then dismisses that risk on the basis of "uncertainties in the data." Notably, EPA provides no explanation of what uncertainties exist in the data. Moreover, to the extent there are uncertainties in EPA's analysis, such uncertainties counsel in favor of a finding of unreasonable risk – EPA could as easily be underestimating the risk presented by these conditions of use as overestimating them. Uncertainty increases the chances of an unreasonable risk; it does not diminish them. Uncertainty, standing alone, does not justify a finding of no unreasonable risk when EPA's own analyses support a finding of unreasonable risk.

To be clear, for one of these facilities, the exceedances EPA calculated were far in excess of the relevant concentration of concern. “The acute RQ associated with this release was 6.46, indicating the surface water concentration was over six times higher than the acute COC.” (p. 287). With respect to chronic exceedances, this facility had an RQ of “188.89 with 250 days of exceedance.” (p. 287). This reflects surface water concentrations nearly 200 times higher than the chronic COC.

C. EPA failed to analyze distribution in commerce and made unsupported risk findings about this condition of use without a supporting analysis.

In the draft risk evaluation, EPA states that “distribution in commerce” “does not present an unreasonable risk,” (p. 437), but EPA makes this finding without *any* supporting analysis. EPA states that a “quantitative evaluation of the distribution of methylene chloride was not included in the risk evaluation because exposures and releases from distribution were considered within each condition of use.” (p. 437). In truth, EPA did not prepare even a *qualitative* evaluation of distribution in commerce of methylene chloride. Notably, unlike the other findings about conditions of use in this table, the finding on distribution in commerce does not cross-reference any other portion of the draft risk evaluation to support its finding, and based on our search of the draft risk evaluation and supplemental documents, nowhere does it appear EPA actually analyzed distribution in commerce. Therefore, 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 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.

EPA excuses its failure to analyze distribution in commerce as a separate condition of use by claiming that it performed this analysis when analyzing the other conditions of use. (pp. 437, 44). But when examining EPA’s analysis of various conditions of use—for example, Manufacturing—EPA does not appear to have actually analyzed the distribution in commerce of methylene chloride as it relates to any of these other conditions of use. (pp. 114-16). We could not find any discussion in the analysis of the other conditions of the use that actually addressed distribution in commerce as an aspect of those conditions of use. Therefore, distribution in commerce may well present an unreasonable risk; EPA simply has not evaluated it at all.

Notably, EPA found that many of these other conditions of use do present an unreasonable risk. (pp. 431-32, 434-63, 465-506). If EPA actually analyzed distribution in commerce when analyzing these conditions of use, EPA does not explain why the finding of unreasonable risk would not equally extend to the distribution in commerce of methylene chloride as parts of these conditions of use. EPA never separately analyzed distribution in commerce as parts of these conditions of use, so EPA does not have a separate analysis of that aspect of the condition of use to support making a different finding.

EPA appears simply to assume that distribution in commerce does not result in any exposures beyond those already related to a given condition of use. EPA provides no analysis or evidence supporting this assumption. Is EPA simply assuming that all distribution occurs through so-called “closed systems” which lead to no releases or exposure whatsoever? EPA has provided no evidence that exposures and releases during distribution will be nonexistent.

The draft risk evaluation and problem formulation also give no attention to potential releases and exposures resulting from accidental releases. EDF does not suggest that EPA needs to consider every possible scenario, but the risk of accidental releases and exposures is very real and certainly “reasonably foreseen” in many respects. For example, as and after Hurricane Harvey passed through Houston, over 40 sites released toxic chemicals into the environment.¹¹³ Given the known accidental releases, the huge number of petrochemical plants and refineries in the Houston area, and the likelihood that flooding there may become more common in light of climate change, such events are clearly reasonably foreseen and hence EPA needs to give more consideration to the potential for accidental releases.

10. Systematic review issues

A. OPPT provides neither explanation nor empirical support for its revisions to the systematic review data quality criteria for epidemiological studies, which make it impossible for epidemiological studies to be scored overall as high quality.

See our comments on this concern in section 6.

B. OPPT’s approach taken to evidence integration in the draft methylene chloride risk evaluation does not align with best practices as reflected and shared by leading systematic review methods for chemical assessment (e.g., OHAT, NavGuide, IRIS).

As we have described in previous comments,¹¹⁴ OPPT has not provided a pre-established methodology for its approach to evidence integration. This violates the agency’s own definition of weight of the scientific evidence; the final rule *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* states that weight of the scientific evidence is:

¹¹³ See, e.g., *More Than 40 Sites Released Hazardous Pollutants Because of Hurricane Harvey*, N.Y. TIMES (Sept. 8, 2017), https://www.nytimes.com/interactive/2017/09/08/us/houston-hurricane-harvey-hazardous-chemicals.html?_r=0.

¹¹⁴ Environmental Defense Fund Comments on Application of Systematic Review in TSCA Risk Evaluations (Aug. 16, 2018), <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2018-0210-0077>; Environmental Defense Fund Comments on Draft Risk Evaluation for C.I. Pigment Violet 29 (Anthra[2,1,9-def:6,5,10-d'e'f']diisoquinoline- 1,3,8,10(2H,9H)-tetrone) (Jan. 14, 2019), <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2018-0604-0013>.

a systematic review method, applied in a manner suited to the nature of the evidence or decision, that uses a *pre-established protocol* to comprehensively, objectively, transparently, and consistently identify and evaluate each stream of evidence, including strengths, limitations, and relevance of each study and to integrate evidence as necessary and appropriate based upon strengths, limitations, and relevance.

As noted in the 2014 National Academy of Sciences (NAS) report that reviewed EPA's IRIS program:

Critical elements of conducting a systematic review include formulating the specific question that will be addressed (problem formulation) and *developing the protocol* that specifies the methods that will be used to address the question (protocol development).¹¹⁵

After the systematic-review questions are specified, protocols for conducting the systematic reviews to address the questions should be developed. *A protocol makes the methods and the process of the review transparent, can provide the opportunity for peer review of the methods, and stands as a record of the review.* It also minimizes bias in evidence identification by ensuring that inclusion of studies in the review does not depend on the studies' findings. Any changes made after the protocol is in place should be transparent, and the rationale for each should be stated. EPA should include protocols for all systematic reviews conducted for a specific IRIS assessment as appendixes to the assessment.¹¹⁶

EPA's IRIS program reflects this NAS recommendation by developing problem formulation and assessment protocols for each of its assessments.¹¹⁷ OPPT needs to develop full protocols for each of its risk evaluation, and should consult with the IRIS program on how best to do so in consideration of requirements under TSCA.

C. EPA's evaluation of study quality is insufficient and inconsistent.

¹¹⁵ Nat'l Research Council, *Review of EPA's Integrated Risk Information System (IRIS) Process* (2014) at p. 5, <https://www.ncbi.nlm.nih.gov/books/NBK230060/> (emphasis added).

¹¹⁶ *Id.* at 6 (emphases added).

¹¹⁷ U.S. EPA, Office of Research & Dev., National Academy of Science Committee to Review Advances Made to the IRIS Program at slide 23 (Feb. 2018), <http://nas-sites.org/dels/files/2018/01/AdIRIS-15.pdf>.

EPA did not consistently evaluate study quality in this draft risk evaluation. For example, in the discussion of Toxicity from Acute/Short-Term Exposure (p. 220), EPA states:

Because EPA didn't develop formal data evaluation criteria for human acute controlled experiments, EPA evaluated these studies in a qualitative manner. This section presents results of animal studies but most were not evaluated for data quality because EPA relied on the human controlled experiments for dose-response and risk estimation and used a single study (Putz et al., 1979) for dose-response. Previous peer-reviewed assessments discuss many of the animal studies, and they are considered acceptable for supporting the weight of scientific evidence for acute endpoints. Several case reports in humans are also describe (*sic*) here but were also not evaluated for quality.

EPA's inconsistent application of its systematic review process results in an arbitrary and capricious analysis.

* * * * *

EDF appreciates the opportunity to provide comments and EPA's consideration of them.