

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

Comments of Safer Chemicals Healthy Families, Natural Resources Defense Council, Earthjustice, and Environmental Health Strategy Center on EPA's Draft Risk Evaluation for Methylene Chloride under Section 6(b) of TSCA

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Safer Chemicals Healthy Families, Natural Resources Defense Council, Earthjustice, and Environmental Health Strategy Center submit these comments on the Environmental Protection Agency (EPA) draft risk evaluation for methylene chloride (MC) under section 6(b) of the Toxic Substances Control Act (TSCA).¹ Our organizations are national and grassroots groups committed to assuring the safety of chemicals used in our homes, workplaces and the many products to which our families and children are exposed each day. We took a leadership role during the TSCA legislative process, advocating the most protective and effective legislation possible to reduce the risks of toxic chemicals in use today.

These comments build on and incorporate by reference our groups' written and oral submissions to the Scientific Advisory Committee on Chemicals (SACC) in connection with its December 3-4 meeting to review the draft MC evaluation.

Executive Summary

The serious risks that MC poses to workers and consumers -- and EPA's slow and inadequate response to these risks -- have long been a source of deep concern to our groups. We were supportive of EPA's 2014 TSCA Work Plan Chemical Risk Assessment for MC in paint strippers and the comprehensive ban on these products that EPA proposed in January 2017. However, new EPA leadership took no action to finalize this ban and four more known deaths occurred during MC paint remover use. With EPA dragging its feet, some of us worked successfully with leading retailers to voluntarily stop sales of paint remover products containing MC and N-Methyl pyrrolidone (NMP). Partnering with the families of young men who died from MC exposure, we also called on EPA to finalize its proposed ban on MC-based paint removers for commercial and consumer use. EPA belatedly issued a final rule banning consumer use of these products in March 2019 but once more delayed protection of exposed workers. Now, we are challenging EPA's failure to ban MC from commercial paint remover products in the Second Circuit Court of Appeals.

As we show below, the draft risk evaluation confirms earlier EPA findings that MC poses serious risks to consumers and workers of death, incapacitating neurotoxic effects, cancer and liver toxicity. More than 8 million workers and several million consumers and bystanders are exposed to these risks. At least 85 deaths have resulted from acute exposure to MC since 1980. By any measure, the dangers from MC exposure are significant, imminent and widespread.

Although the findings of the draft evaluation are alarming, we believe that EPA has in fact significantly understated MC's risks because of several omissions and errors in its risk determinations. Many of these flaws mirror shortcomings in earlier draft evaluations for other chemicals that were identified in SACC

¹ 84 Federal Register 57866 (October 29, 2019); https://www.epa.gov/sites/production/files/2019-10/documents/1_methylene_chloride_risk_evaluation_peer_review_draft_heronet_public.pdf (MC Risk Evaluation).

reports. It is disappointing that the SACC's concerns and recommendations have not been heeded by the Agency and addressed in later draft evaluations for MC and other chemicals. EPA must incorporate SACC feedback in its final evaluations and, if it disagrees with specific comments, provide a detailed rationale for its position. EPA's current approach to risk evaluations – as evidenced by the six draft evaluations released thus far – threaten the integrity of the TSCA program and make the Agency's actions legally vulnerable. Its actions could delay meaningful progress on protecting the public from toxic chemicals for years to come, the exact opposite of what Congress intended when it strengthened TSCA in 2016.

Our concerns about the draft evaluation and recommendations for addressing them are as follows:

- *The Draft Evaluation Again Demonstrates Serious Acute and Chronic Risks to Workers and Consumers but EPA Is Not Taking Timely Action*
 - Drawing heavily on EPA's earlier analysis of MC paint removers, the draft risk evaluation broadens the findings of its 2014 risk assessment to include the many other consumer and commercial uses of MC.
 - The draft concludes that, for nearly all exposed workers and consumers, these additional uses present serious acute and chronic risks that, like the paint remover uses EPA proposed to ban in 2017, are unreasonable under TSCA.
 - We have urged EPA to immediately warn the public of these risks and require manufacturers to protect workers and consumers from harm rather than delay action for several years while EPA finalizes its risk evaluation and completes rulemaking under section 6(a) of TSCA.
 - EPA's refusal to act now will mean more avoidable cases of serious harm and death from MC exposure.
- *The Draft Risk Evaluation Fails to Account for Multiple Sources of Exposure by Consumers and Workers*
 - EPA does not combine inhalation and dermal exposures, even though they occur concurrently, and thus fails to account for their combined contribution to total risk.
 - EPA makes no effort to examine aggregate risk from multiple pathways, such as concurrent workplace, consumer product, and environmental exposures, which are common for many individuals and communities.
- *EPA's Exclusion of All Environmental Releases Violates TSCA and Disregards Additional Human Exposure Pathways that Contribute to Aggregate Exposure and Risk*
 - EPA excludes all MC environmental releases in determining human exposure, including air emissions, which are unusually large and account for elevated ambient air concentrations in many urban areas.
 - Removing all environmental exposure pathways from risk evaluations is contrary to the plain language and structure of TSCA and will defeat the central purpose of TSCA reform.
 - SACC has repeatedly raised concern about EPA's failure to consider environmental pathways of human exposure.
 - The air, water and waste pathways excluded from the MC evaluation are significant contributors to human exposure.
- *EPA Correctly Recognizes that MC is a Non-Threshold Carcinogen but Understates and Discounts Its Cancer Risks*

- The extensive evidence that MC is genotoxic demonstrates that it is unlikely to have a threshold Mode of Action (MOA) and therefore requires linear low-dose extrapolation under EPA's risk assessment guidelines for carcinogenicity.
 - EPA's assessment of cancer risk unjustifiably excludes all evidence of carcinogenicity except for liver and lung tumors, thereby failing to consider epidemiological data that show associations between Non-Hodgkin's Lymphoma (NHL) and biliary cancers and MC exposure as well as statistically significant increases in mammary tumors in animal studies.
 - EPA has not explained and justified why the Inhalation Unit Risk (IUR) for carcinogenicity in its draft evaluation is significantly lower than in previous MC evaluations.
 - In determining the 99th percentile IUR, EPA uses a less protective approach than its IRIS assessment to account for the higher prevalence of the GST-T1 genotype in certain population subgroups; it has thus failed to fully consider cancer risks to "potentially exposed or susceptible subpopulations" as TSCA requires.
 - The draft risk evaluation declines to assess cancer risks from acute exposure even though it is widely recognized that genotoxic carcinogens like MC can induce cancer following a limited exposure event and that methods to estimate acute cancer risks using chronic data are available.
 - The evaluation also fails to address cancer risks to consumers from chronic exposure to MC, disregarding plausible scenarios of recurring and/or multiple consumer product use.
 - EPA continues to use a cancer risk of 1×10^{-4} as the benchmark for determining unreasonable risk to workers, notwithstanding the Agency's repeated articulation of 1×10^{-6} as the public health goal for all its programs.
- *The Draft Evaluation Inadequately Addresses Risks to Vulnerable Populations and Fails to Apply Sufficient Uncertainty Factors*
 - EPA's 10X Uncertainty Factor (UF) for intra-species variability is not sufficient to account for the increased susceptibility to MC's acute effects of pregnant women, the elderly, fetuses, children, people engaged in vigorous physical activity, users of alcohol and individuals suffering from lung and heart disease.
 - EPA's understatement of acute risks to vulnerable subpopulations is compounded by an inadequate UF for extrapolating from a LOAEL to a NOAEL.
 - EPA's benchmark MOE of 10 for MC's non-cancer chronic effects is inadequate because it unjustifiably reduces UFs for intraspecies and interspecies variability to 3 from the customary values of 10.
 - EPA's benchmark MOE for chronic effects should include a further UF of at least 10 for database uncertainty to account for the lack of adequate data on developmental neurotoxicity, immunotoxicity, developmental/reproductive effects and endocrine effects.
 - For endpoints that EPA believes lacks sufficient data for risk determinations, it should immediately use its TSCA testing authorities to obtain the necessary information and determine whether MC presents an unreasonable risk for those endpoints.
 - *EPA's Unreasonable Risk Determinations for Workers Are Under-Protective Because They Assume a Level of Personal Protective Equipment (PPE) Use that Lacks Any Basis in Workplace Practice, Law and Policy*
 - EPA itself acknowledges the absence of real-world evidence that workers consistently wear respirators and gloves.

- In each of its reviews of draft evaluations, the SACC has raised concerns that EPA’s reliance on PPE for determinations of unreasonable risk is unsupported and contrary to established principles of worker protection.
- OSHA regulations and policy do not support EPA’s claims that PPE use is adequately protective.
- Consistent with the OSHA/NIOSH “hierarchy of controls,” the determinations of unreasonable risk in EPA’s final risk evaluation should be based on anticipated workplace exposure levels *in the absence of PPE*.
- *EPA Lacks Sufficient Exposure Data to Support Proposed Findings of No Unreasonable Risk to Workers*
 - In those cases where EPA found that workers were not at unreasonable risk, it relied on monitoring performed by industry while largely ignoring OSHA samples of workplace exposure.
 - The Agency also failed to use its TSCA authorities to obtain available worker exposure information from industry and state and federal agencies.
 - In finalizing the MC risk evaluation, EPA should make every effort to obtain additional workplace monitoring data from OSHA, state agencies and industry and should use all available data to determine unreasonable risks to workers.
- *EPA’s Draft Evaluation Unjustifiably Downplays and Mischaracterizes its Own Occupational Risk Determinations.*
 - EPA repeatedly finds that risks that fall below its benchmark MOEs for acute and chronic effects or exceed its cancer risk benchmarks are nonetheless “reasonable” and do not warrant further worker protection.
 - EPA’s flawed risk characterizations occur most frequently for so-called occupational non-users, or “ONUs,” for whom EPA defends ignoring risks that are greater than its benchmark levels by citing “uncertainties” in its estimates of exposure.
- *EPA Unjustifiably Concludes that MC Does Not Present Unreasonable Environmental Risks and Fails to Address Critical Environmental Impacts*
 - EPA concludes that MC does not pose unreasonable ecological risks by excluding the studies that demonstrate the greatest toxicity, obscuring the results of the studies that it does consider, and disregarding risk quotients more than 100 times greater than EPA’s unreasonable risk threshold.
 - EPA fails to account for the foreseeable effects of climate change, notwithstanding the SACC’s recognition that temperature increases will influence important risk evaluation inputs, such as vapor pressure, water solubility, and Henry’s law constants
 - EPA fails to address MC’s recognized ozone depleting properties despite the risks of ozone depletion to both human health and the environment.
- *EPA’s TSCA “Systematic Review” Method Is Deeply Flawed and Will Compromise the Quality, Validity and Protectiveness of EPA’s Ongoing Risk Evaluations.*
 - The TSCA method departs radically from accepted scientific principles for systematic review adopted by the Institute of Medicine (IOM), the National Toxicology Program (NTP) and

EPA's Integrated Risk Information System (IRIS) and endorsed by the NAS and other peer review bodies.

- The SACC has "noted problems with both the systematic review design and consistent implementation of its protocols" and called upon EPA to make significant changes in approach.
- Thus far, the serious concerns raised by SACC have not been addressed by EPA: at a minimum, EPA's final risk evaluations must respond fully to the SACC's comments and implement its recommendations.
- While the National Academy of Sciences (NAS) reviews the TSCA method, EPA should not use it in any of its risk evaluations but should instead apply one of the recognized systematic review methodologies.

I. The Draft MC Evaluation Again Demonstrates Serious Acute and Chronic Risks to Workers and Consumers

EPA's concerns about the acute and chronic hazards of MC are long-standing. The Agency began a priority review of MC's health effects under TSCA in 1985.² In 2011, EPA's Integrated Risk Information System (IRIS) issued a final MC toxicity assessment³ and in 2014, the Agency finalized its TSCA risk assessment for MC-based paint removers.⁴ Because of the serious risks demonstrated in that assessment, EPA proposed in early 2017 to ban these products under TSCA for both consumer and commercial use.⁵ However, EPA dragged its feet on finalizing this proposal, and four more deaths occurred from inhalation of MC fumes during paint remover use. Following a public outcry and pleas by the families of the decedents, EPA belatedly finalized its consumer use ban in March of this year but again took no action to protect workers using MC paint strippers despite earlier commitments of its then-Administrator to finalize the 2017 proposal in its entirety.⁶

Drawing on its earlier scientific analysis, the draft risk evaluation broadens the findings of the 2014 risk assessment to include many other consumer and commercial uses of MC. The population exposed to MC from these uses is extremely large, totaling more than 8 million workers and several million consumers and exposed bystanders.⁷

² EPA, Methylene Chloride; Initiation of Accelerated Review Under TSCA Section 4(f), 50 Fed. Reg. 20126 (May 14, 1985).

³ Toxicological Review of Dichloromethane (Methylene Chloride) (CASRN 75-09-2) in Support of Summary Information on the Integrated Risk Information System (IRIS) [EPA IRIS Assessment]. (EPA/635/R-10/003F). Washington, D.C. <http://www.epa.gov/iris/toxreviews/0070tr.pdf> U.

⁴ TSCA Work Plan Chemical Risk Assessment, Methylene Chloride: Paint Stripping Use. (740-R1-4003). Environmental Protection Agency, Office of Chemical Safety and Pollution Prevention. https://www.epa.gov/sites/production/files/2015-09/documents/dcm_opptworkplanra_final.pdf {Workplan Risk Assessment}

⁵ 82 Fed. Reg. 7464 (January 19, 2017).

⁶ 84 Fed. Reg. 11420 (March 23, 2019).

⁷ The risk evaluation provides estimates of exposed workers for each of the commercial/industrial conditions of use it examines and these estimates total over 8 million for all exposed workers. EPA's 2017 paint remover proposal estimated that 1.3 consumers were exposed to these products (82 Fed. Reg. 7475-6). An even larger number of consumers are probably exposed to the 15 consumer products addressed by the draft evaluation although EPA does not estimate the size of this population.

As EPA has earlier found, the draft risk evaluation concludes that “[r]isks from acute exposures include central nervous system risks such as central nervous system depression and a decrease in peripheral vision, each of which can lead to workplace accidents and which are precursors to more severe central nervous system effects such as incapacitation, loss of consciousness, and death” (p. 30). These effects occur because MC fumes act as a CNS depressant and also metabolize in the body into carbon monoxide (CO), cutting off the supply of oxygen and killing users in as few as ten minutes. According to a recent analysis (attached) by scientists at the University of California San Francisco, 85 deaths have been linked to acute exposure to MC since 1980. This likely understates the actual number; EPA indicated in its 2017 proposed rule that numerous additional deaths were probably either unreported or erroneously attributed to other causes.⁸

The draft risk evaluation also concludes that MC has serious chronic health effects. It determines that “[t]here is sufficient evidence of methylene chloride carcinogenicity from animal studies” and that the chemical has produced tumors at multiple sites, in males and females, in rats and mice, by oral and inhalation exposure, and in multiple studies.” (p. 264). It further finds that “inhalation and oral studies identified liver effects as a sensitive non-cancer effect linked with exposure to methylene chloride in animals.” (p. 260)

The draft evaluation addresses 15 consumer products that contain MC. It concludes that these products present acute risks similar in nature and magnitude to the paint remover risks on which EPA based its consumer use ban. *Specifically, for all but one of the 15 products, projected acute exposures in one or more of EPA’s use scenarios were above or alarmingly close to MC levels causing neurotoxic effects in human studies.* (p.36) As a result, for inhalation or dermal exposure or both, margins of exposure (MOE) were well below the “benchmark MOE” that EPA used to define unreasonable risk. For several of the products, the MOEs were unprotective not only for product users but for consumer bystanders as well.

The risks to workers identified in the draft evaluation were equally alarming. *The evaluation found inhalation and/or dermal MOEs below the benchmark MOE for at least one exposure scenario for all 31 of the industrial and commercial conditions of use it analyzed.* (pp. 34-36) These conditions include the commercial use of MC-containing paint removers (pp. 685-725). The risk evaluation incorporates verbatim large portions of EPA’s 2014 risk assessment and thus reaffirms the rationale for the proposed ban on commercial use of these products that EPA failed to finalize earlier this year.

On November 8, 2019, twenty groups, including these commenters, wrote to EPA Administrator Wheeler to emphasize that the dangers to consumers and workers of acute exposure to MC are too great to delay action while EPA finalizes its risk evaluation and completes rulemaking under section 6(a) of TSCA. The letter (copy attached) urged EPA to immediately warn the public of these risks and require manufacturers to protect workers and consumers from harm. It also urged the Agency to immediately finalize its proposed ban on commercial use of MC-containing paint removers since the draft evaluation once again reaffirms that this use presents unreasonable risks of injury. Although EPA has not formally responded to our letter, Assistant Administrator Dunn announced at the December 3-4, 2019 SACC meeting that EPA has no plans to put in place immediate protections against MC’s acute health risks. EPA’s inaction will mean more avoidable cases of serious harm and death from MC exposure as several more years pass before EPA completes its risk evaluation and finalizes rules restricting MC use.

⁸ 82 Fed. Reg. 7482.

II. The Draft Risk Evaluation Fails to Account for Multiple Sources of Exposure by Consumers and Workers

Although the draft evaluation demonstrates that MC presents serious and unreasonable risks to health, its risk determinations examine individual sources of exposure in isolation and fail to estimate the overall risks to consumers and workers from these exposure sources combined. Aggregation of multiple pathways that contribute to individual exposure would result in even smaller margins of exposure (MOEs) for acute and non-cancer chronic effects and larger carcinogenicity risks under MC's conditions of use.

A. EPA Fails to Combine Concurrent Inhalation and Dermal Exposures

The draft risk evaluation concludes that MOEs for acute dermal and inhalation exposure are below benchmark MOEs for several worker and consumer use scenarios. (Table 4-104) EPA also calculates cancer risks for both inhalation and dermal exposure. The inhalation cancer risks are in many cases higher than 1×10^{-4} ; the dermal risks are above 1×10^{-6} and in some cases 1×10^{-5} in glove scenarios. (Table 4-71)⁹ EPA recognizes (p. 387) that “[i]nhalation and dermal exposures are assumed to occur simultaneously for workers and consumers,” explaining that:

“For workplace exposures inhalation and dermal exposures are assumed to occur simultaneously i.e., both occur at the start of the task and continue through the end of the task, shift, or workday. For household exposures inhalation and dermal exposures occur at the start of the task and continue through the end of the task. Consumer inhalation exposures typically continue for some time after the task is complete, although at a lower concentration, while the individual remains in the rest of house. (p. 387)

Nonetheless, EPA did not aggregate exposures across these routes and calculate a total risk accounting for the contribution of both. (p. 304) EPA acknowledges that this approach “may lead to an underestimate of exposure.” However, it explains that it “chose not to employ simple additivity of exposure [routes] . . . because of the uncertainties present in the current exposure estimation procedures.” Id.

It is not clear what “uncertainties” EPA is referring to. In fact, EPA derived dermal PODs by extrapolation from inhalation Points of Departure (PODs), using toxicokinetic information to estimate dermal doses at which the effects seen in inhalation studies would occur, as explained below:

“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. The inhalation PODs were extrapolated using a POD based on either human data i.e., acute exposures or the BMDL_{HEC} a value from animals adjusted to account for animal to human extrapolation using the PBPK model the preferred approach because this incorporates methylene chloride specific toxicokinetic data. Therefore, the equations for extrapolating from inhalation PODs to the dermal route account for human inhalation and body weight, shown below, assume average exposure factors from the Exposure Factors Handbook . . .” (p. 282)

⁹ Because both dermal and inhalation risks are significant, there is no basis for disregarding dermal exposures on the grounds that inhalation is the predominant source of risk, as erroneously suggested by EPA in the draft evaluation (p. 387).

Since EPA had sufficient confidence in route-to-route extrapolation to base estimates of dermal risk on the results of inhalation studies, it is hard to understand why this same approach could not be used to determine overall exposure by the two routes combined.¹⁰ Thus, EPA's MOEs and cancer risk estimates should have been based on exposure levels reflecting the contribution of each route, as opposed to calculating risks for each route individually. This would result in substantially lower MOEs and higher estimated cancer risks for use scenarios where both dermal and inhalation exposures are concurrent.

In its report on the draft evaluation for 1-bromopropane (1-BP), SACC recommended that EPA estimate "cumulative exposures, which involves both dermal and inhalation contact with 1-BP" because "dermal exposure to 1-BP would most likely correspond with simultaneous inhalation exposure" and "vapor and dermal exposures are not separable."¹¹ **EPA should similarly use combined dermal and inhalation exposures to determine MC's risks in its final evaluation.**

B. EPA Must Aggregate Exposures that Occur in Workplaces and Consumer Settings

Given the large number of commercial and consumer uses of MC, workers in MC user facilities may also be exposed to MC in their homes. This may occur, for example, when they perform paint removal or furniture refinishing projects or use one or more other MC-containing household products, such as spot removers, shoe polish, adhesives and sealants. Families of workers may also have "take home" exposures, i.e. contact with the worker's contaminated clothing or skin. Workers may also do weekend work or have a side business using the same skills – and the same toxic products – as during their weekday work, thus extending their exposure time. For individuals exposed to MC in multiple settings, risks would be a function of the aggregate contribution of each route to total exposure. However, the draft evaluation looks at each exposure pathway in isolation from others, thus ignoring people with exposure to MC both in the workplace and at home.

The SACC report on the 1-BP evaluation indicates that:

"The Committee found that the draft risk evaluation failed to consider cumulative or aggregate exposures. It was pointed out that a worker who is occupationally exposed may also be exposed through other conditions of use in the home. Yet, these exposures are decoupled in the draft risk evaluation. The Committee was concerned that 1-BP off-gassing from insulation in home and schools is inadequately assessed, thereby underestimating exposures."¹²

Section 6(b)(4)(F)(ii) of TSCA requires EPA risk evaluations to "describe whether aggregate or sentinel

¹⁰ If there is any uncertainty, it involves the absence of toxicity data for the dermal route of exposure, which leaves open the possibility that extrapolations from inhalation data understate MC's adverse effects from dermal application. This could be considered a "data-base deficiency" warranting an additional UF in determining a benchmark MOE for acute and chronic dermal exposure. See pp. 27-29 *infra*.

¹¹ TSCA Science Advisory Committee on Chemicals Meeting Minutes and Final Report No. 2019-03, Peer Review for the United States Environmental Protection Agency (EPA) Draft Risk Evaluation for 1-Bromopropane (1-BP) (SACC Report on 1-BP), December 12, 2019, <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0235-0061>, at 47, 73.

¹² *Id.*, at 16.

exposures to a chemical substance under the conditions of use were considered, and the basis for that consideration.” The MC draft indicates that that EPA used an “aggregate exposure” methodology by estimating dermal and inhalation risks for each condition of use (even though it failed to combine them) but ignores the possibility of concurrent exposure to MC *across conditions of use*.¹³ This is an unwarranted departure from EPA’s own definition of aggregate exposure as “the combined exposures to an individual from a single chemical substance across multiple routes and across multiple pathways” (40 CFR § 702.33). **A true assessment of MC’s risks would have determined combined exposures from inhalation and dermal exposure during each condition of use (i.e. “across multiple routes”) and from different conditions of use (i.e. “across multiple pathways”). EPA should include this assessment in its final MC evaluation.**

III. EPA’s Exclusion of All Environmental Releases Violates TSCA and Disregards Additional Human Exposure Pathways that Contribute to Aggregate Exposure and Risk

EPA’s failure to conduct an aggregate exposure assessment is compounded by its blanket exclusion of all environmental releases from its draft evaluation, resulting in the absence of any consideration of environmental pathways that contribute to overall human risk exposure and risk. This approach is an unlawful interpretation of TSCA, has twice been rejected by SACC and overlooks the widespread presence of MC in environmental media to which millions of people are exposed.

A. Removing All Environmental Exposure Pathways from Risk Evaluations Is Contrary to the Plain Language and Structure of TSCA and Will Defeat the Central Purpose of TSCA Reform

As in prior risk evaluations, EPA justifies excluding the contribution of environmental releases to total MC exposure as follows:

“As part of the problem formulation for methylene chloride, EPA identified exposure pathways under other environmental statutes, administered by EPA, which adequately assess and effectively manage exposures and for which long-standing regulatory and analytical processes already exist, i.e., the Clean Air Act (CAA), the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA) and the Resource Conservation and Recovery Act (RCRA). The Office of Chemical Safety and Pollution Prevention works closely with EPA offices that administer and implement the regulatory programs under these statutes. In some cases, EPA has determined 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. EPA believes that the TSCA risk evaluation should focus on those exposure pathways associated with TSCA uses that are not subject to the regulatory regimes discussed above because these pathways are likely to represent the greatest areas of concern to EPA.” (p. 428)

This rationale is contrary to the comprehensive multi-media scope of TSCA.

Under section 6(b)(4)(A), TSCA risk evaluations must determine “whether a chemical substance presents an unreasonable risk of injury to health or the environment” – a requirement that entails examining all sources of exposure to the substance. Similarly, section 6(b)(4)(A) provides that a risk evaluation must determine

¹³ MC Draft Evaluation at 387.

the substance's risks under "the conditions of use." This broad term spans the entire life cycle of a chemical and is defined under section 3(4) to mean "the circumstances . . . under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of." These "circumstances" clearly include air emissions and releases to water that result in pathways of human exposure and risk, whether or not they might be addressed under other laws.

Other provisions in section 6 confirm the need to consider environmental releases as part of chemical risk evaluations. For example, storage near significant sources of drinking water is a factor that EPA must examine in its process for designating chemicals as high- or low-priority under section 6(b)(1)(A). Similarly, under both this provision and section 6(b)(2)(D), chemicals with significant potential for persistence, bioaccumulation and toxicity (PBTs) must receive preference in the selection of substances for high-priority listing. PBTs are of concern because of their presence in environmental media and potential to concentrate in animals and humans as they are distributed in air, water and soil taken up the food chain. If EPA does not consider environmental release pathways of PBTs in evaluating their risks, it would be pointless to designate them as high priority since the ensuing evaluation could not meaningfully address the contribution of environmental exposure pathways to total risk.

If Congress had intended a blanket exemption of environmental releases from risk evaluations under section 6(b), it surely would have said so explicitly, given the far-reaching impact of such an exemption. But as the legislative history of the original law confirms, Congress recognized that then-existing environmental laws were "clearly inadequate" to address the "serious risks of harm" to public health from toxic chemicals. H.R. Rep. No. 94-1341, 94th Cong., 2d Sess. at 7 (1976); see S. Rep. No. 94-698, 94TH Cong., 2d Sess. (1976) at 3 ("[W]e have become literally surrounded by a manmade chemical environment. ... [T]oo frequently, we have discovered that certain of these chemicals present lethal health and environmental dangers."). While other federal environmental laws focused on specific media, such as air or water, none gave EPA authority to "look comprehensively" at the hazards of a chemical "in total." S. Rep. No. 94-698, at 2. Congress designed TSCA to fill these "regulatory gaps," *id.* at 1, through a comprehensive approach to chemical risk management that considered "the full extent of human or environmental exposure," H.R. Rep. No. 94-1341, at 6.

In amending TSCA in 2016, Congress sought to promote "effective implementation" of the 1976 law's objectives. See S. Rep. No. 114-67, 114th Cong., 1st Sess. (2015) at 2. At the time it strengthened TSCA, Congress affirmed that the intent of the original law—to give EPA "authority to look at the hazards [of chemicals] in total," S. Rep. No. 94-698, at 2—remained "intact." S. Rep. No. 114-67, at 7. Indeed, in a statement accompanying the law's passage, its Senate Democratic sponsors underscored that, with the expanded authorities conferred by Congress, TSCA should not be "construed as a 'gap filler' statutory authority of last resort" but "as the primary statute for the regulation of toxic substances."¹⁴

EPA's position that other environmental laws should displace TSCA risk evaluations arbitrarily assumes that these laws provide equivalent protection of public health and the environment and that there is no added benefit in evaluating the risks presented by environmental pathways of exposure under TSCA. However, in reality, these other laws vary greatly in the degree of protection they afford against chemical risks and the extent of their application to unsafe chemicals. These limitations are precisely why Congress gave EPA comprehensive authority over chemical risks under TSCA in 1976 and strengthened that authority in 2016.

¹⁴ Congressional Record – Senate 3517 (June 7, 2016).

TSCA's strict risk-based framework for chemical risk management is not mirrored in most environmental laws that govern releases to air, water and soil and disposal of waste. For example, the standard-setting process to establish discharge limits for chemical and other pollutants under the Clean Water Act (CWA) is technology-based and does not require the elimination of all unreasonable risk.¹⁵ The same is true of several provisions of the Clean Air Act (CAA) that regulate emissions from new and modified stationary sources of pollution and mobile sources.¹⁶ Even statutes that do allow for consideration of risks also direct EPA to weigh cost and other economic factors. The Safe Drinking Water Act (SDWA), for example, requires cost-benefit analysis in setting limits for drinking water contaminants, the very approach rejected in the 2016 TSCA amendments.¹⁷ And importantly, most of these laws do not include TSCA's explicit protections for potentially exposed or susceptible subpopulations at higher risk than the general population. Equally important, even if other laws provided the high level of protection required under TSCA, they narrowly focus on single media pathways of exposure and thus would not provide the cross-media, multi-pathway assessment of exposure and risk that Congress required under TSCA.

B. SACC Has Repeatedly Raised Concern About the Failure to Consider Environmental Pathways of Human Exposure

in its review of the 1,4-dioxane draft, the SACC questioned EPA's rationale for failing to consider environmental pathways of exposure:¹⁸

“Exposure scenarios that include consumers are important given the known presence of 1,4-Dioxane in plastics, other commercially available products, surface water, drinking water, groundwater, and in sediments. The Committee also had concerns that the omission of these multiple routes of exposure puts workers who inhale or ingest 1,4-Dioxane outside the workplace at even greater risk.”

The SACC added that:¹⁹

“The Committee discussed that if each program office of the EPA says others are assessing the risks and thus not including them in their assessment, the U.S. public will be left with no overall assessment of risks. If risks have been assessed by other program offices of EPA then the Agency should present them as part of the underlying data to support this TSCA Evaluation—if not, the Agency must gather the data for an assessment or include an assessment based on the assumption of near-worst-case exposures.”

The SACC underscored that “[g]eneral human population and biota exposure must be assessed for inhalation, ingestion, and dermal routes [and that] [d]ifferent sub-populations may have different extents of exposure, but each route must be assessed.”²⁰ EPA's narrower approach, it said, “strayed from basic risk assessment principles by omitting well known exposure routes such as water

¹⁵ 33 U.S.C. §1317.

¹⁶ 42 U.S.C. §§7411,7475.

¹⁷ 42 U.S.C. §300g-1

¹⁸ 1,4-Dioxane and HBCD SACC Report, at 18.

¹⁹ *Id.*

²⁰ *Id.*

consumption by all occupationally and non-occupationally-exposed humans as well as similar exposures to other biological receptors.”²¹

The SACC review of the 1-BP draft similarly took EPA to task for failing to consider air emissions and other environmental releases:²²

“The lack of consideration for general population exposures excludes a vast extent of the US population (workers, consumers, school children, and other populations) who are exposed to 1-BP, perhaps on a daily basis. The lack of consideration of the general population exposure is concerning given the strong evidence of widespread exposure to a chemical that may be 1-BP based (from biomonitoring data).”

C. The Environmental Pathways Excluded from the MC Evaluation are Significant Contributors to Human Exposure

The MC risk evaluation ignores – in the SACC’s words – basic “risk assessment principles” by excluding “well-known exposure routes” and failing to provide an “overall assessment of risks.” For example, consumers who use MC-based products may also be exposed to MC air emissions, particularly if they live near emitting facilities, and may also be exposed to MC through drinking water or proximity to waste sites. Similarly, workers exposed to MC at their places of employment may also inhale MC from ambient air or breathe vapors from MC-containing products used in their homes, adding to their overall exposure.

Air Emissions. According to the EPA Problem Formulation,²³ “[i]nhalation serves as the expected primary route of exposure for the general population due to both [MC’s] volatility and propensity to be released to air from ongoing commercial and industrial activities.” (p.39) Because MC is frequently applied as a solvent in open processes, significant loss of vapors to the atmosphere is expected. The most recent round of reporting for the Toxics Release Inventory (TRI) showed MC air emissions of 2.9 million pounds in 2018.²⁴ Since emissions below the TRI reporting thresholds are not captured in the TRI data-base, this figure does not reflect the emissions of the many small commercial operations that use MC as a solvent; it thus underestimates total releases to air. According to the 2000 ATSDR toxicological profile:

“It has been estimated that 85% of the total amount of methylene chloride produced in the United States is lost to the environment (EPA 1985e), about 86% of which is released to the atmosphere (EPA 1982a). Thus, about 73% (370 million pounds) of the U.S. production volume for 1988 (500 million pounds), of methylene chloride was lost to the atmosphere in 1988.”²⁵

Because of these releases, the Problem Formulation finds that “levels of methylene chloride in the ambient air are widespread and shown to be increasing.” (p. 39) Not unexpectedly, ambient levels tend to be highest in urban areas with a concentration of MC user facilities. According to the MC problem formulation, the “2011 National Air Toxics Assessment (NATA) modeled concentrations for various air toxics nationwide at a census tract level. This screening level tool modeled a maximum total methylene chloride concentration of

²¹ Id.

²² SACC 1-BP Report at 17.

²³ https://www.epa.gov/sites/production/files/2018-06/documents/mecl_problem_formulation_05-31-18.pdf (EPA Problem Formulation).

²⁴ EPA, 2018 TRI Factsheet: Chemical – Dichloromethane, <https://iaspub.epa.gov/triexplorer/chemical.html?pYear=2018&pLoc=000075092&pParent=TRI&pDataSet=TRIQ1>.

²⁵ <https://www.atsdr.cdc.gov/toxprofiles/tp14.pdf>, at 178.

5,000 parts per trillion (18 µg/m³) and maximum human inhalation exposure concentrations of 3,900 parts per trillion (14 µg/m³).” (p. 36) ATSDR reports that:

“Methylene chloride was among the chemicals monitored in a statewide survey of hazardous air pollutants by the Arizona Hazardous Air Pollutants Monitoring Program. The average amount of methylene chloride detected in air ranged from 0.61 ppm on a hillside in Yavapai County to 1.62 ppm in Phoenix (Zielinska et al. 1998). Concentrations of methylene chloride in urban areas and in the vicinity of hazardous waste sites are generally one to two orders of magnitude higher.”²⁶

ATSDR emphasizes that “groups within the general population that could have potentially high exposures . . . include individuals living in proximity to sites where methylene chloride was produced or sites where methylene chloride was disposed, and individuals living near 1 of the 1,569 NPL hazardous waste sites where methylene chloride has been detected in some environmental media (HazDat 1996).”²⁷ Similarly, the EPA MC Problem Formulation notes that “[o]ther groups of individuals within the general population . . . may experience greater exposures due to their proximity to conditions of use . . . that result in releases to the environment and subsequent exposures (e.g., individuals who live or work near manufacturing, processing, use or disposal sites).” (p. 40) Although these considerations indicate that communities near MC-emitting facilities or waste sites should be treated as “potentially exposed or susceptible subpopulations” in the MC risk evaluation, EPA at no point estimates their higher levels of exposure and the elevated risks that result.

MC’s status as a CAA Hazardous Air Pollutant (“HAP”) under the CAA does not justify ignoring air emissions in the draft evaluation. Title III of the CAA initially mandates technology-based -- not risk based – emission limits. Once these limits are in place, the law gives EPA at least eight more years to evaluate residual risks and potentially set risk-based emission standards under CAA section 112(f).²⁸ However, these standards would only consider emission-related risks, and thus would not take into account aggregate health risks from all sources of exposure. Moreover, the CAA mandates emission standards for “major” sources, which are defined as facilities that emit more than 10 tons per year of any single HAP or 25 tons per year of all HAPs.²⁹ This definition would likely not cover the thousands of smaller establishments that in the aggregate account for substantial MC air emissions. These facilities may be regulated as “area sources” under the CAA but would not be subject to mandatory, chemical-specific risk-based standards.

It is revealing that, in a 2007 CAA Title III rulemaking to limit emissions of MC, trichloroethylene and perchloroethylene (PCE) during halogenated solvent cleaning operations,³⁰ EPA acknowledged that its standards 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 . . . between 500,000 and 1,000,000.”³¹ This is clear evidence that CAA regulation of MC air emissions has not eliminated unreasonable cancer risks under TSCA, much less accounted for the contribution of emitting facilities to overall sources of exposure and risk.

²⁶ Id at 183.

²⁷ Id at 189.

²⁸ 42 U.S.C. § 7412(f)(2).

²⁹ 42 U.S.C. § 7412(a)(1).

³⁰ National Air Emission Standards for Hazardous Air Pollutants: Halogenated Solvent Cleaning, 85 Fed. Reg. 25138 (May 3, 2007).

³¹ Id. at 25,148.

In short, TSCA's role in assessing these aggregate risk and exposure pathways is unique and not duplicated in other statutes and must be reflected in the MC risk evaluation.

Other Environmental Exposure Scenarios. According to the EPA Problem Formulation, “[m]ethylene chloride has been detected in ground water and surface water, including finished drinking water, through varied national monitoring efforts and water quality databases.” (p. 36) The problem formulation also indicates that, according to 2015 TRI reports, “271 facilities reported a total of about 153.7 million pounds of methylene chloride waste managed. Of this total, about 96.9 million pounds were recycled, 15.6 million pounds were recovered for energy, [and] 37.8 million pounds were treated.” (Id.) Of the TRI reported amounts released to the environment in 2015, 114,000 pounds were land disposed (including at hazardous waste landfills) and 713,000 pounds were released in other forms such as to waste brokers.³² ATSDR indicates that “occurrence of methylene chloride in groundwater has been reported in several surveys across the United States . . . [and] the compound was the sixth most frequently detected organic contaminant found in groundwater during hazardous waste disposal site investigations with a detection frequency of 19%.”³³ These data suggest the high frequency of MC spills and releases at abandoned waste sites and manufacturing and processing sites. ATSDR also notes that MC was “detected in 20% of 338 sediment samples recorded in the STORET database”³⁴ – additional evidence of spills and releases during plant operations and disposal.

In its report on the 1,4-dioxane risk evaluation, the SACC wrote that “EPA should also include a spill scenario as potential and probable occurrences in the occupational environment.”³⁵ This recommendation is well-grounded in TSCA, which requires EPA to consider not only known and intended but reasonably foreseen exposures and also highlights the need to examine proximity to drinking water sources during prioritization in section 6(b)(1)(A). However, the MC risk evaluation does not evaluate exposures from reasonably foreseen spills and leaks during production, use, distribution and disposal.

In its report on the 1,4-dioxane and HBCD risk evaluations, the SACC noted EPA's failure to consider releases associated with disposal, including “the movement and breakdown of disposed materials from soils and in particular from landfills into air and waterways.”³⁶ The findings described above confirm that these are important pathways for MC as well. In its recent decision on the EPA framework rule for risk evaluations, the Ninth Circuit ruled that “TSCA's definition of ‘conditions of use’ clearly includes uses and future disposals of chemicals,” as well as “spills, leaks, and other uncontrolled discharges” that may occur during facility operations or from landfills or abandoned waste sites.³⁷ While EPA has claimed discretion to exclude from risk evaluations conditions of use (including environmental releases) that are subject to other laws, the Ninth Circuit decision also holds that EPA lacks such discretion under its risk evaluation rule. It concludes that “we do not interpret the language in the Rule to say anything about exclusion of conditions of use” and that “[w]e therefore conclude that the challenged provisions

³² Id.

³³ ATSDR, at 185.

³⁴ Id.

³⁵ TSCA Science Advisory Committee on Chemicals Meeting Minutes and Final Report No. 2019-02 *Peer Review for EPA Draft Risk Evaluations for 1,4-Dioxane and Cyclic Aliphatic Bromide Cluster (HBCD)*, November 1, 2019, at 18 (1,4-Dioxane and HBCD SACC Report), at 27, available at <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0238-0063>.

³⁶ Id. at 113.

³⁷ *Safer Chemicals, Healthy Families v USEPA*, No. 17-72260 (9th Cir. Nov. 14, 2019), at 55-57.

unambiguously do not grant EPA the discretion” to remove such conditions from the scope of risk evaluations.³⁸

In sum, the final MC risk evaluation must consider environmental releases along with all other pathways of exposure and determine their combined contribution to aggregate exposure and risk.

IV. EPA Correctly Recognizes that MC is a Non-Threshold Carcinogen but Understates and Discounts Cancer Risks

As EPA recognizes in its draft evaluation, “[t]here 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.” (p. 264) Based on this evidence, MC has been classified as likely to be carcinogenic to humans by the International Agency for Research on Cancer (IARC),³⁹ the National Toxicology Program (NTP) *Report on Carcinogens*⁴⁰ and the 2011 EPA IRIS Assessment.⁴¹

As discussed below, EPA correctly rejected claims that MC has a non-linear mode of action (MOA) but nonetheless failed to account for the full magnitude of MC’s cancer risks and set a “benchmark” for unreasonable cancer risk to workers that is at variance with TSCA and longstanding EPA policy.

A. All Evidence Indicates that MC Is a Non-Threshold Carcinogen Requiring Linear Low-Dose Extrapolation

The draft risk evaluation concludes that there is extensive evidence of a genotoxic MOA for MC carcinogenicity:

“Mechanistic data show that methylene chloride has a mutagenic MOA involving DNA-reactive metabolites produced via a metabolic pathway catalyzed by GSTT1 (U.S. EPA, 2011). There are numerous genotoxicity tests showing positive results for methylene chloride, including assays for mutagenicity in bacteria and mutagenicity, DNA damage, and clastogenicity in mammalian tissues in vitro and in vivo (IARC, 2016; U.S. EPA, 2011). The most strongly positive results in mammalian tissues in vivo and in vitro were found in mouse lung and liver, tissues with the greatest rates of GST metabolism and the highest susceptibility to methylene chloride-induced tumors. To further strengthen the case for the role of GST-mediated metabolism, studies have demonstrated increases in damage with the addition of GSTT1 to the test system and decreases in damage by addition of a GSH depletory. The GSTT1 metabolic pathway has been measured in human tissues with activities that are lower than rodents. Thus, the cancer results in animal studies are relevant to humans, who do exhibit some GSTT1 activity (U.S. EPA, 2011).

³⁸ *Id.*, at 43.

³⁹ 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>.

⁴⁰ NTP, *Report on carcinogens Monograph for dichloromethane* at p. 1, <https://ntp.niehs.nih.gov/ntp/roc/content/profiles/dichloromethane.pdf>.

⁴¹ EPA, Toxicological Review Of Dichloromethane (Methylene Chloride) (CAS No. 75-09-2) In Support of Summary Information on the Integrated Risk Information System (IRIS), November 2011, at https://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/0070tr.pdf (MC IRIS Assessment).

In particular, human cells have exhibited genotoxicity without exogenous addition of GSTT1 (U.S. EPA, 2011).” (pp. 265-66)

Relying heavily on the 2011 IRIS assessment, EPA rejected “sustained cell proliferation as an alternative MOA for methylene chloride-induced lung and liver cancer,” explaining that “data were not identified suggesting a receptor-mediated mode (e.g., peroxisome proliferation resulting from PPAR- α activation; enzyme induction by CAR, PXR, or AhR activation).” (p. 266). On this basis, EPA concludes that “[a]vailable data do not suggest that modes of action other than genotoxicity are relevant.” (p. 247)

EPA’s 2005 Guidelines for Carcinogen Risk Assessment⁴² emphasize the high level of evidence necessary to depart from the presumption of linearity for carcinogens:

“Elucidation of a mode of action for a particular cancer response in animals or humans is a data-rich determination. *Significant information should be developed to ensure that a scientifically justifiable mode of action underlies the process leading to cancer at a given site. In the absence of sufficiently, scientifically justifiable mode of action information, EPA generally takes public health protective, default positions* regarding the interpretation of toxicologic and epidemiologic data animal tumor findings are judged to be relevant to humans, and cancer risks are assumed to conform with low dose linearity” (emphasis added) (1-10 through 1-11).

The Guidelines add 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. *Nonlinear approaches generally should not be used in cases where the mode of action has not been ascertained.* (emphasis added) (3-21)

A nonlinear approach should be selected when there are sufficient data to ascertain the mode of action and conclude that it is not linear at low doses and the agent does not demonstrate mutagenic or other activity consistent with linearity at low doses.” (3-22).

EPA has correctly applied these principles in the draft evaluation to conclude that MC should be considered a non-threshold, linear carcinogen.

B. EPA Has Unjustifiably Excluded from its Evaluation All Evidence of Carcinogenicity Except for Liver and Lung Tumors

EPA’s cancer risk estimate is based on liver and lung tumors in mice (Mennear et al. 1988 which is the published version of the NTP 1986 study). Using these data sets for risk modeling approaches is consistent with the earlier IRIS 2011 and TSCA 2014 evaluations. However, we are greatly concerned by EPA’s failure to address risks of other cancer types, and its dismissal of evidence due to the kinds of limitations that are routine in epidemiologic studies (such as small numbers or co-exposure to other carcinogens). Using a systematic review framework, these limitations can be addressed using standard

⁴² EPA 2005. Guidelines for Carcinogen Risk Assessment. at 84-85. Available at https://www.epa.gov/sites/production/files/2013-09/documents/cancer_guidelines_final_3-25-05.pdf

statistical adjustments, by considering all the evidence across many studies, and by considering supporting evidence from animal studies and other streams of evidence. Instead, the EPA TSCA program fails to apply modern epidemiologic methods of analysis. For example, instead of using mechanistic evidence to support limited evidence of cancer in human or animal studies (as done by IARC and other reputable chemical assessment programs), the EPA TSCA program dismisses such evidence as inconclusive without taking into account mechanistic considerations. The result is an underestimate of cancer risks.

The draft MC evaluation makes a passing mention of the finding of biliary cancers in some epidemiologic studies, including a study in Japanese print workers, but dismisses these data as not demonstrating a cancer risk (p. 247; Kumagai et al, 2016). However, a recent IARC assessment came to the opposite conclusion, noting that cancers of the biliary tract are normally very rare, making the incidences in the epidemiologic studies “very high” (IARC Vol 110; MC draft risk evaluation Section 5.2).⁴³ IARC concluded that, “high risk of this rare cancer in one cohort study of workers without exposures to other likely risk factors and among exposed printing workers in Japan is consistent with a causal association,” although noting that there were some potential confounders including low case numbers and exposure to 1,2-dichloropropane (IARC Vol 110, Section 5.2). However, both these confounders would make it harder to see a link with cancer⁴⁴— they would bias to the null – thus increasing our confidence in the observation of a causal link between MC and biliary cancer.

IARC also identified a potential elevated risk of NHL cancers from MC exposures, noting that “positive associations for NHL were consistent among studies using different study designs and in several countries” (IARC, Section 5.2). While exposure to other toxic solvents is acknowledged as a potential confounder in these studies, IARC concluded that the epidemiologic evidence was “limited” for both biliary tract and NHL cancers in its final assessment (IARC, Section 6). IARC defines “limited” as suggesting a carcinogenic effect but not enough by itself to make a definitive evaluation. Limited evidence as defined by IARC should carry sufficient weight to merit inclusion in a quantitative risk estimate, with appropriate adjustment factors. Further, leading economists and scientists recommend including health effects with less certain evidence in risk assessments as the foundational theory of benefit cost analysis “supports inclusion and accounting for less certain health risks.”⁴⁵ According to the EPA draft evaluation, “Mennear et al. (1988) (which is the published version of NTP (1986)) and Aiso et al. (2014a) each reported an increased incidence of mononuclear cell leukemia in female (but not male) rats (Table 3-13) [but] the incidences did not exhibit monotonic dose-response relationships.” (p. 254).⁴⁶ On this basis, EPA dismissed the risk of NHL and did not include it in the Agency’s cancer risk estimate.

EPA also disregarded breast (mammary) cancer risks, despite acknowledging that, “animal studies consistently identify methylene chloride exposure as associated with mammary tumors” (p. 381). In

⁴³ IARC 2016. Some Chemicals Used as Solvents and in Polymer Manufacture. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 110

⁴⁴ Gee D. Late lessons from early warnings: Toward realism and precaution with endocrine-disrupting substances. *Environ Health Perspect.* 2006 Apr;114 Suppl 1:152-60. Review

⁴⁵ McGartland, A., Revesz, R., Axelrad, D. A., Dockins, C., Sutton, P., & Woodruff, T. J. (2017). Estimating the health benefits of environmental regulations. *Science*, 357(6350), 457–458. <https://doi.org/10.1126/science.aam8204>

⁴⁶ EPA’s draft evaluation considers the studies that report a risk of NHL and other hematopoietic tumors to be high or medium quality studies (Table 3-12, p. 255).

fact, the data from animal studies is very compelling. An NTP 1986 2-year inhalation study in F344 rats identified a statistically significant positive trend when mammary gland adenoma and fibroadenomas were combined (females: 5/50, 11/50, 13/50, 23/50). A later rodent inhalation study by Aiso et al 2014 reported that the incidence of fibroadenoma of the mammary gland was significantly increased in males at the highest dose and with a positive trend in females (see data Table 3-11). EPA also noted that a fraction of the fibroadenomas lead to carcinomas, and that “breast cancer has been identified in one human epidemiology study.” (p. 381) Moreover, EPA reported that had it used these data to develop an IUR, it would have been more protective than the combined liver and lung tumor IURs (Table 3-20 on p. 279-280, p. 381). Despite this evidence of breast cancer risks, EPA failed to base the IUR on this endpoint for the following three reasons: (1) only a small number of tumors in animal studies progressed to malignancy; (2) the dose-metric was not certain; and (3) data on mutagenicity in these tissues is lacking. These considerations are inappropriate, unscientific, and inconsistent with EPA’s Guidelines for the following reasons:

- First, many tumors in animal studies may not progress to malignancy within the two-year observation period of the study. This is because a 2-year old rat is roughly equivalent to a 60-year old person, whereas about 80 percent of cancer in people occurs after age 60. Thus, a conventional two-year bioassay, as was conducted for MC, does not have a sufficient latency period to detect many cancers.⁴⁷ In fact, the National Cancer Institute (NCI) reports that among U.S. women, the average age of breast cancer diagnosis is 62, with death from breast cancer at 68 years old.⁴⁸ This means that roughly half of breast cancers that will lead to deaths in women would occur outside the two-year testing period of the rodent studies. For this reason, EPA’s Cancer Guidelines state, “*The default is to include benign tumors observed in animal studies in the assessment of animal tumor incidence, if such tumors have the capacity to progress to the malignancies with which they are associated.*” This default is consistent with the approach of the National Toxicology Program and the International Agency for Research on Cancer and is more protective of public health than not including benign tumors in the assessment; benign and malignant tumors are treated as representative of related responses to the test agent (McConnell et al., 1986), which is scientifically appropriate.” (Cancer Guidelines, p. A-5, italics in original). Consistent with its own Guidelines and scientific best practices, EPA should treat any tumors capable of progressing to malignancy as evidence of cancer risk.
- Second, the uncertainty in the dose-metric could have been addressed with UFs. EPA recognizes that uncertainty in risk estimates is a frequent occurrence and references the NAS in its discussion in the Cancer Guidelines, recommending that in the face of uncertainties, EPA should “present not only point estimates of risk, but also the sources and magnitudes of uncertainty associated with these estimates” (Cancer Guidelines, p. 1-4). The Cancer Guidelines notes that this could encourage

⁴⁷ Huff J, Jacobson MF, Davis DL. The Limits of Two-Year Bioassay Exposure Regimens for Identifying Chemical Carcinogens. *Environmental Health Perspectives*. 2008;116(11):1439-1442. The authors present evidence demonstrating that ceasing exposure at 2 years without monitoring tumor development for additional time cannot estimate the impact of food additives, drugs, and other chemicals on humans who die in their 70s or later. The authors argue that is why scientists at the National Institutes of Environmental Health Sciences (NIEHS) reject the notion that an 18 month rodent bioassay (about 30-50 years in human age) is long enough to reliably predict cancer risks (Bucher 2002; Haseman et al. 2001; Kodell et al. 2000).

⁴⁸ National Cancer Institute, Cancer Stat Facts: Female Breast Cancer.
<https://seer.cancer.gov/statfacts/html/breast.html>

research to address uncertainties. In fact, EPA should use its authority under TSCA to require such research.

- Third, mutagenicity does not have to be identified in each tumor type for it to be considered cancer. As the Cancer Guidelines note, “There are many examples of possible modes of carcinogenic action, such as mutagenicity, mitogenesis, inhibition of cell death, cytotoxicity with reparative cell proliferation, and immune suppression.” (Cancer Guidelines, p. 1-10, footnote #2). The Cancer Guidelines make clear that, “In the absence of sufficiently, scientifically justifiable mode of action information, EPA generally takes public health protective, default positions regarding the interpretation of toxicologic and epidemiologic data: animal tumor findings are judged to be relevant to humans, and cancer risks are assumed to conform with low dose linearity.” (Cancer Guidelines, p. 1-10, 11)

EPA’s disregard of the breast cancer risks is inappropriate. EPA should have used the IUR it calculates for mammary tumors as a basis for its cancer risk estimates.

In sum, EPA’s draft evaluation acknowledges that there are relevant studies reporting cancers of the liver, lung, breast, brain and central nervous system, and most types of hematopoietic (blood cell) cancers (p. 264). However, in every case where EPA cannot make “firm conclusions regarding the specific association between methylene chloride and the outcomes,” the risk findings are not included in the cancer risk estimate (p. 264).

In its final risk evaluation, EPA should quantitatively include the mammary, NHL and biliary cancer risks from MC exposure, and other cancer risks, with additional adjustment factors.

C. EPA Has Not Justified Using a Lower IUR Than It Used in its 2011 IRIS and 2014 TSCA Assessments

The Inhalation Unit Risk (IUR) for cancer in the draft risk evaluation is 1.38×10^{-6} per mg/m^3 . (p. 304) In the 2014 EPA assessment, the IUR was 1×10^{-5} per mg/m^3 ,⁴⁹ based on dose-response modeling in the 2011 IRIS assessment, which uses the same IUR.⁵⁰ The differences in the IURs mean that the cancer risk estimates in the 2014 assessment are 6-7 times greater than in the draft evaluation. The draft evaluation does not explain how and why the two IURs are different beyond briefly acknowledging that EPA’s IUR modeling has changed from 2014. It is troubling that EPA has departed from two final, peer reviewed assessments without transparently justifying this significant change in approach.

One possible explanation of the different IURs may involve polymorphisms, genetic factors that may increase susceptibility to cancer for some portion of the population. The IRIS assessment explains that a –

“major pathway for dichloromethane metabolism involves the conjugation of dichloromethane to GSH, catalyzed by GST. This results in the formation of a GSH conjugate that is eventually metabolized to CO₂ (Figure 3-1). The conjugation of dichloromethane to GSH results in

⁴⁹ Workplan Risk Assessment, at 68.

⁵⁰ EPA IRIS Assessment, at 271.

formation of two reactive intermediates that have been proposed to be involved in dichloromethane toxicity, S-(chloromethyl)glutathione and formaldehyde.”(p.14)

The assessment states that “[r]esults from studies of GST-T1 genotypes in human blood samples indicate that average prevalences of the GST-T1 null (-/-) genotype are higher in Asian ethnic groups (47–64%) than in other groups, including Caucasians (19–20%), African-Americans (22%), and mixed groups (19%).” (p. 15) Noting that “the known polymorphisms for GST-T1 expression were integrated into the human model,” it then explains that the “distributions of human inhalation unit risk values (from which the recommended [i.e., mean] values were taken) show that the 99th percentiles are approximately seven- and six-fold higher than means for liver and lung cancer, respectively.” (p.253)

EPA’s draft risk evaluation further suggests that it used the full distribution of GSTT genotypes in the human population in determining the 99th percentile IUR:

“Sampling of the full distribution of GSTT genotypes in the human population (GSTT1+/, GSTT1+/- and GSTT1 -/-) was done to derive the IUR for liver and lung tumors” ... Use of the upper-bound estimate for the full population distribution of the GSTT1 genotypes is considered sufficiently protective of sensitive sub-populations.” (p. 659)

The IRIS assessment, however, rejected this approach, as described in its discussion under the subheading of, “*Consideration of Sensitive Human Subpopulations*”:

“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.” (p.220)

Carriers of the GST-T1(+/) genotype would be a “potentially exposed or susceptible subpopulation” under TSCA (and according to the EPA IRIS assessment, p. 220) and thus EPA is required to determine whether the cancer risk to these subgroups (as opposed to the general population) is unreasonable. This dictates looking at the upper bound distribution of GST-T1 genotypes in vulnerable populations who require the greatest protection – the opposite of what EPA in fact did.

EPA should follow the IRIS-recommended approach in its final evaluation and adjust the IUR accordingly. It should also provide a fuller explanation of all the differences in the IUR calculation in the draft risk evaluation as compared to the 2011 and 2014 IURs and how they impacted the estimates of cancer risk.

D. EPA’s Risk Evaluation Should Account for Acute Cancer Risks to Workers and Consumers

The draft risk evaluation declines to assess cancer risks from acute exposure on the ground that a “[r]elationship is not known between a single short-term exposure to DCM and the induction of cancer in humans.” (p.699) However, it is widely recognized that genotoxic carcinogens like MC can induce

cancer following a limited acute exposure event and that methods to estimate such risks are available. As stated in a 2011 National Research Council (NRC) report:⁵¹

“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.”

Thus, there exists a recognized methodology for extrapolating from findings of carcinogenicity in long-term studies to exposures of short duration. Rather than summarily dismissing acute cancer risks as impossible to estimate, EPA should have quantified these risks using the framework outlined by NRC.

Because EPA did not assess acute cancer risks, its draft evaluation omits any consideration of carcinogenicity endpoints that might impact consumers as a result of short-term exposure. This omission could be interpreted to mean that consumers have no risk of cancer even though MC’s genotoxic MOA suggests the contrary. While EPA estimates chronic cancer risks to workers, the draft evaluation provides no indication that acute exposure could also lead to carcinogenic effects and thus fails to address the risks to workers of such exposure. **EPA’s final risk evaluation should address acute cancer risks to consumers and workers.**

E. EPA Should Address Chronic Cancer Risks to Consumers

The draft risk evaluation also fails to address cancer risks to consumers from chronic exposure to MC. This omission disregards use scenarios for consumer products that could result in repeated MC exposure over time. The risk evaluation identifies 15 separate categories of MC-containing products. (pp. 174-174). Some of these products (adhesives, adhesive removers, brush cleaners and sealants) would be expected to be used regularly by hobbyists, artists who work at home or home renovators. Others (Automotive AC Leak Sealer, Automotive AC Refrigerant, Carburetor Cleaner, Engine Cleaner) would likely be used frequently by consumers who maintain and repair their own or friends’ vehicles. Indeed, it is likely that many consumers use multiple MC-containing products over time.

⁵¹ NRC, *Standard Operating Procedures for Developing Acute Exposure Guideline Levels for Hazardous Chemicals*, pp. 111-112 (2001), available at <https://www.epa.gov/aegl/standing-operating-procedures-developing-acute-exposure-guideline-levels-aegls-hazardous>

EPA's 1-BP draft evaluation acknowledged that it is not realistic to assume that consumers are only exposed once to consumer products containing this substance in view of how these products are used:⁵²

"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."

These considerations would be equally applicable to MC. In fact, the MC problem formulation commits EPA to evaluate risks to "subsets of consumers who may use commercially-available products or those who may use products more frequently than typical consumers." (p. 65) Unaccountably, the MC draft evaluation does not follow through on this commitment even though it acknowledges that "[f]or all product scenarios, both acute and chronic exposures were expected to occur." (p. 169)

EPA's final evaluation must address chronic cancer risks to consumers based on scenarios of recurring and/or multiple consumer product use.⁵³

F. EPA Should Use a Benchmark of 1×10^{-6} to Determine Whether Cancer Risks to Workers and Consumers are Unreasonable under TSCA

As with earlier evaluations, EPA continues to use a cancer risk of 1×10^{-4} as the benchmark for determining unreasonable risk to workers. Using this benchmark results in a significantly smaller number of worker exposure scenarios that present unreasonable risks than under cancer risk levels of 1×10^{-5} and 1×10^{-6} . The SACC has previously stated that EPA has not provided "adequate explanation and justification" for this reduced threshold⁵⁴ and the MC draft evaluation also fails to justify EPA's approach.

The draft MC evaluation describes (p. 426) how EPA has previously approached cancer risks under the laws it administers as follows:

"Standard cancer benchmarks used by EPA and other regulatory agencies are an increased cancer risk above benchmarks ranging from 1 in 1,000,000 to 1 in 10,000 (i.e., 1×10^{-6} to 1×10^{-4}) depending on the subpopulation exposed. Generally, EPA considers 1×10^{-6} to 1×10^{-4} as the appropriate benchmark for the general population, consumer users, and non-occupational PESS."

Thus, as EPA notes, in applying CAA "residual risk" standards for air toxics, it uses a two-step approach that includes a "presumptive limit on maximum individual lifetime [cancer] risk (MIR) of approximately 1 in 10 thousand" and consideration of whether emissions standards provide an ample margin of safety to protect public health "in consideration of all health information, including the number of persons at risk levels higher than approximately 1 in 1 million, as well as other relevant

⁵² 1-BP Draft Evaluation at 130.

⁵³ Similarly, the evaluation should address non-cancer chronic risks to consumers, such as neurotoxicity and liver effects.

⁵⁴ SACC 1,4-Dioxane and HBCD Report at 23.

factors.”⁵⁵ EPA likewise uses a risk range of 1×10^{-4} to 1×10^{-6} to set cleanup goals at CERCLA hazardous waste sites.⁵⁶ In fact, EPA has used a 1×10^{-6} cancer standard to evaluate risk and determine CERCLA remedies at sites where methylene chloride is one of the principal contaminants of concern.⁵⁷

Despite reserving discretion to make case-by-case decisions within this range, however, EPA has identified 1×10^{-6} as its goal for public health protection. Thus, in its air toxics standard for radionuclides, EPA stressed that it “should reduce risks to less than 1×10^{-6} for as many exposed people as reasonably possible.”⁵⁸ Similarly, in guidance for setting health-based water quality criteria under the Clean Water Act (CWA), EPA explained that it:⁵⁹

“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.”

In the CERCLA program, EPA guidance provides that, while “remedies should reduce the risks from carcinogenic contaminants such that the excess cumulative individual lifetime cancer risk for site-related exposures falls between 10-4 and 10-6,” the Agency “has expressed a preference for cleanups achieving the more protective end of the risk range (i.e., 10-6).”⁶⁰

However, EPA’s recent draft risk evaluations deviate from this approach for worker exposures, maintaining that risks smaller than 1×10^{-4} will be considered “reasonable” under TSCA because, “consistent with case law and 2017 NIOSH guidance,” this risk level applies to “industrial and commercial work environments subject to Occupational Safety and Health Act (OSHA) requirements.” (p. 426)

EPA fails to explain why OSHA precedent should control decision-making under TSCA, a separate law with different purposes and wording. The cancer risk threshold applied by NIOSH and OSHA is rooted in the Supreme Court’s *Benzene* decision, which interpreted the OSH Act as requiring “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 (1980) (emphasis added). The Court grounded this interpretation in an examination of the language, structure and legislative history of the OSH Act. TSCA, by contrast, is anchored in the concept of “unreasonable risk” (a term that implies a lower risk threshold than the OSH Act concept of “significant risk”). No provision of TSCA provides that workers should receive less protection than other exposed subpopulations or that well-established EPA benchmarks for unacceptable cancer risks would be inapplicable to workers. Indeed, workers are specifically identified as a “potentially exposed or susceptible subpopulation” that EPA is required to protect in section 3(12) of TSCA, indicating that

⁵⁵ 54 Fed. Reg. 38044, 38045 (September 14, 1989).

⁵⁶ USEPA, *Rules of Thumb For Superfund Remedy Selection*, August 1997, found at <https://semspub.epa.gov/work/HQ/174931.pdf>. (CERCLA Guidance).

⁵⁷ See Record of Decision, Bofors Nobel Superfund Site at 12 (Sept. 1990).

⁵⁸ 54 Fed. Reg. 51654, 51686 (Dec. 15, 1989).

⁵⁹ 106 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>.

⁶⁰ CERCLA Guidance at 9.

Congress was particularly concerned by the levels of toxic chemicals in the workplace and the special vulnerability of some employee populations to their adverse health effects.

Moreover, in contrast to the OSH Act, TSCA provides protections to workers not just from chemical exposure in the workplace but from air emissions and other environmental releases as well as exposures to consumer products. As discussed above, while draft EPA risk evaluations have assessed worker exposure in isolation from other pathways, this approach understates risks; instead, EPA should combine exposures from all relevant pathways and determine an aggregate risk reflecting the contribution of each source. This is a further reason why setting a higher cancer risk threshold for workers than other populations is unjustified under TSCA.

EPA must apply to workers the same benchmarks for determining unreasonable cancer risks that it uses for other populations. For all exposed populations, the goal should be to protect against cancer risks exceeding 1×10^{-6} .

V. The Draft Evaluation Inadequately Addresses Risks to Vulnerable Populations and Fails to Apply Sufficient Uncertainty Factors

EPA also understates MC's risks because it fails to adequately protect vulnerable populations and does not use all necessary uncertainty factors (UFs) in calculating benchmark MOEs.⁶¹

A. Numerous Population Subgroups Groups Are at Increased Risk of MC's Acute Effects

Of particular concern is the greater vulnerability of certain population subgroups to the risks of central nervous system (CNS) depression, coma and death from acute exposure to MC. As EPA's evaluation indicates, these groups include pregnant women, the elderly, fetuses, children, people engaged in vigorous physical activity, users of alcohol and Individuals suffering from lung and heart disease (pp. 274-275).

For example, the draft indicates that "EPA considers that increased COHb levels resulting from inhalation exposure to methylene chloride may also result in adverse effects in individuals with cardiac disease, a sensitive subpopulation." (p.259). EPA indicates that a smaller increase in COHb (between 2.5 and 4.5%) may precipitate angina than the increase (5.1%) at which neurotoxic symptoms were observed in Putz et al. (1979), the key human study EPA used as its POD for acute effects. (p. 275) Thus, unsafe MC concentrations would be lower for heart patients than for healthy individuals in the general population.

EPA also explained that:

"Fetuses, infants and toddlers are also potentially susceptible to methylene chloride exposure. 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 in infants with higher residual levels of fetal hemoglobin when exposed to high concentrations of methylene

⁶¹ According to a recent NAS report, "[f]ive UFs are considered to account for uncertainties associated with intrahuman variability, extrapolation of animal data to humans, extrapolation of subchronic exposure data to chronic exposure scenarios, use of a LOAEL instead of a NOAEL, and database deficiencies." National Academies of Sciences, Engineering, and Medicine 2019. *Review of DOD's Approach to Deriving an Occupational Exposure Level for Trichloroethylene*. Washington, DC: The National Academies Press. <https://doi.org/10.17226/25610>, at 44.

chloride. (OEHHA, 2008b). Alexeeff and Kilgore (1983) identified an age-related difference in nervous system responses among mice as well.” (p.387)

These groups, too, may be harmed by smaller CO increases, at lower exposure levels, than healthy adults.

Underscoring the risks to fetuses is evidence that MC crosses the placental barrier. As the 2011 IRIS assessment (p. 9) finds:

“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, 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.”

The draft MC evaluation does not mention placental transfer as an additional risk factor for fetuses. Because fetuses are already more vulnerable to the neurotoxic effects of elevated CO than healthy adults, even where fetal exposures may be lower than maternal exposures, the effects on the fetus are likely to be much more severe and even deadly. Use of an additional UF to address to address greater susceptibility to MC’s CNS effects during early-life exposure is consistent with the similarly enhanced UFs recommended in EPA’s Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens.⁶²

EPA attempted to account for the enhanced susceptibility of these groups by applying a default intraspecies uncertainty/variability factor (UF) of 10 (p. 274). However, this UF is customarily used by EPA to account for normal expected variations in sensitivity within the healthy population.⁶³ Here, by contrast, EPA has identified specific subgroups with biological characteristics that make it likely that they will experience adverse acute effects at lower concentrations than healthy adults.⁶⁴ **To provide protection to these groups, a UF beyond the default intraspecies 10X factor should be applied, as EPA**

⁶² U.S. EPA. Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens. U.S. Environmental Protection Agency, Washington, DC, EPA/630/R-03/003F, 2005.

<https://www.epa.gov/risk/supplemental-guidance-assessing-susceptibility-early-life-exposure-carcinogens>

⁶³ For instance, in its draft Pigment Violet 29 risk evaluation EPA used an intraspecies UF of 10 despite finding “no evidence of increased susceptibility for any single group relative to the general population.” 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) (Nov. 2018), found at https://www.epa.gov/sites/production/files/2018-11/documents/draft_pv29_risk_evaluation_public.pdf (PV29 Risk Evaluation).

⁶⁴ Thus, EPA guidance provides that “a 10-fold factor may sometimes be too small because of factors that can influence large differences in susceptibility, such as genetic polymorphisms.” EPA-630-P02-002F, A Review of the Reference Dose and Reference Concentration Processes, at 4-44(Dec. 2002) <https://www.epa.gov/risk/review-reference-dose-and-reference-concentration-processes-document>. (RD and RC Review).

has done for other susceptible groups such as infants and children.⁶⁵ We recommend a UF of at least 20X, consistent with the EPA Supplemental Cancer Guidance.

B. EPA's Understatement of Acute Risks to Vulnerable Subpopulations is Compounded by An Inadequate UF for Extrapolating from a LOAEL to a NOAEL

In addition to applying an inadequate UF for intraspecies variation, EPA's benchmark MOE for acute effects reflects an inadequate UF for extrapolation from a Lowest Adverse Effects Level (LOAEL) to a No Adverse Effects Level (NOAEL). EPA only applies a 3-fold UF. (p. 274) Under standard EPA practice, however, the default LOAEL-to-NOAEL UF is 10.⁶⁶ EPA claims that it reduced that uncertainty factor "because the effects observed" in the study used to calculate acute non-cancer risks "are of a small magnitude," namely, a 7% decrease in peripheral vision after 1.5 hours of exposure. (Id.) However, the effects observed in that study are not "of a small magnitude." In addition to a reduction in peripheral vision, which presents serious risks to many of the commercial and consumer users of methylene chloride, the study reported a Carboxyhemoglobin ("COHb") level in exposed subjects of 5.1%.⁶⁷ The Acute Exposure Guideline Level ("AEG") analysis of MC reports that COHb levels of 4% can lead to "disabling" effects,⁶⁸ and EPA's draft risk evaluation states that "at COHb levels of 2 or 4%, patients with coronary artery disease may experience a reduced time until onset of angina (chest pain) during physical exertion." (Id. at 275) EPA fails to explain why reduced peripheral vision, earlier onset of angina, and "disabling" effects are considered to be "of a small magnitude."

Moreover, even if an adjustment in the LOAEL-to-NOAEL uncertainty factor were warranted, EPA has not justified the decrease from 10 to 3. When EPA assessed MC's paint stripping uses in 2014, it used that exact same study to calculate acute non-cancer risks and applied a LOAEL-to-NOAEL uncertainty factor of 6.⁶⁹ The effects observed in that study have not changed over the last five years, yet EPA decided, without explanation, to further reduce that uncertainty factor and cut its benchmark MOE in half.

EPA should use a UF of 10 for LOAEL-to-NOAEL extrapolation. Together with a UF of 20 for intra-species variability, this would result in a benchmark MOE of at least 200 for acute effects as compared to the value of 30 in the draft evaluation.

C. EPA's UF for MC's Non-Cancer Chronic Effects Is Inadequate

For MC's chronic non-cancer risks, EPA calculates a benchmark MOE of 10 based on a 3-fold UF for interspecies variability and a 3-fold UF for intraspecies variability. (p. 278–79) This is a significant

⁶⁵ EPA, Consideration of the FQPA Safety Factor and Other Uncertainty Factors In Cumulative Risk Assessment of Chemicals Sharing a Common Mechanism of Toxicity, February 28, 2002, available at <https://www.epa.gov/sites/production/files/2015-07/documents/apps-10x-sf-for-cra.pdf>; Assessing susceptibility from early-life exposure to carcinogens. Environ Health Perspect. 2005;113(9):1125-33. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1280390/>

RD and RC Review at 4-44.

⁶⁷ Draft MC Risk Evaluation at 275; EPA, Methylene Chloride Interim Acute Exposure Guideline Levels 10 (Dec. 2008), https://www.epa.gov/sites/production/files/201408/documents/methylene_chloride_interim_dec_2008_v1.pdf.

⁶⁸ Id. at viii–ix.

⁶⁹ TSCA Work Plan Chemical Risk Assessment, at 76–77.

departure from standard EPA practice, under which the default value for both of those UFs is 10, and their combined benchmark MOE would typically be 100.⁷⁰

Reducing the interspecies variability UF is warranted only where there is evidence of correspondence between human and animal response. Thus, in its report on the 1,4-dioxane risk evaluation, the SACC wrote that “[c]onsidering statements about the lack of data in some of the human studies, despite some degree of correspondence between effects observed in humans and experimental animals, the [interspecies UF] of 3 seems unjustified; a full value of 10 seems more appropriate.”⁷¹ Similarly, for MC, EPA found considerable evidence of liver effects in rodents but virtually no human evidence or information on the MOA for liver toxicity. (p. 260)

EPA guidance likewise cautions against reductions in the 10X UF for intraspecies variability: “reduction of the intraspecies UF from a default of 10 [should] be considered only if data are sufficiently representative of the exposure/dose-response data for the most susceptible subpopulation(s).”⁷² However, there is no basis for assuming that experimental animal data on MC’s liver toxicity in fact account for variability in response among the different human subpopulations who may be vulnerable to liver effects, such as people with high alcohol consumption or impaired liver function.

Because EPA has provided no basis for reducing these UFs, the benchmark MOE for MC’s non-cancer chronic effects should be increased to 100.

D. Based on its Own Recognition of Inadequate Data for Several Endpoints, EPA Should Add an Uncertainty Factor of 10 for Database Uncertainty

EPA has consistently recognized that, despite data raising concerns for several endpoints, critical gaps exist in understanding of MC’s human health effects. These data gaps are called out in the 2011 IRIS assessment and TSCA risk evaluation, but the latter fails to recognize the implications of these uncertainties for EPA’s determinations of risk and to include a UF to reflect them.

According to the IRIS MC assessment, “[t]he inhalation database lacks adequate developmental neurotoxicity and immunotoxicity studies at chronic low exposures.” (p. 264) IRIS explains the need for developmental neurotoxicity data as follows:

“One data uncertainty identified is the potential for neurodevelopmental effects. Animal bioassays have not identified gross or microscopic effects on neural tissues from long-term exposures or single (Schwetz et al., 1975) or multigenerational (Nitschke et al., 1988b) developmental toxicity studies, albeit with the limitations regarding dosing protocol. However, behavioral changes were observed in pups born to rats exposed to high levels (4,500 ppm) of dichloromethane (Bornschein et al., 1980; Hardin and Manson, 1980); 4,500 ppm was the only dose used in this study. Thus, uncertainty exists as to the development of neurological effects from lower gestational exposures in animals or in humans.” (p. 264)

In the case of immunotoxicity, IRIS says that:

⁷⁰ RD and RC Review at 4-42 to 4-44.

⁷¹ SACC 1,4-Dioxane and HBCD Report at 70.

⁷² Id.

“An acute, 3-hour exposure to 100 ppm dichloromethane demonstrated evidence of immunosuppression in CD-1 mice (Aranyi et al., 1986). This study used a functional immune assay that is relevant to humans (i.e., increased risk of Streptococcal pneumonia-related mortality and decreased clearance of Klebsiella bacteria). Chronic and/or repeated exposure studies evaluating functional immunity are not available and represent a data gap.” (pp. 263-64)

The EPA evaluation echoes this concern, explaining that the Agency “did not carry immune system effects forward for dose-response because epidemiological, animal and mechanistic data are limited and inconclusive.” (p.380)

The EPA evaluation also highlights the insufficiency of reproductive/developmental toxicity data, noting that “although some studies identify reproductive and developmental effects, epidemiological studies lacked controls for co-exposures, animal studies observed effects mostly at higher methylene chloride concentrations in animals and EPA identified no relevant mechanistic information.” (p. 263) The findings of the available studies -- including heart defects in children, reduced fertility, and spontaneous abortions – signaled the need for further investigation but because this work was not carried out, EPA dismissed the findings as inconclusive.

Neither the IRIS assessment nor the draft risk evaluation for MC contains any mention of potential endocrine effects even though the European Chemicals Agency lists MC as “possibly endocrine disrupting”⁷³ and it is also listed on the Endocrine Disruption Exchange’s List of Potential Endocrine Disruptors, which “identifies chemicals that have shown evidence of endocrine disruption in scientific research.”⁷⁴ The lack of endocrine effects data is another area of data insufficiency for MC.

EPA guidance calls for application of a UF where the absence of adequate data creates uncertainty in determining a chemical’s health effects:⁷⁵

“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.”

⁷³ ECHA, Hazardous Substance Information: Dichloromethane. <https://echa.europa.eu/substance-information/-/substanceinfo/100.000.763>.

⁷⁴ About the TEDX List, The Endocrine Disruption Exchange, <https://endocrinedisruption.org/interactive-tools/tedx-list-of-potential-endocrine-disruptors/about-the-tedx-list> (last visited Nov. 21, 2019). See also TEDX Listings for Methylene Chloride, <https://endocrinedisruption.org/interactive-tools/tedx-list-of-potential-endocrine-disruptors/search-the-tedx-list> (enter the chemical name and click Search).

⁷⁵ RD and RC Review at 4-44

The size of this UF can vary between 3 and 10. EPA guidance advises that “the size of the database factor to be applied will depend on other information in the database and on how much impact the missing data may have on determining the toxicity of a chemical and, consequently, the POD.”⁷⁶

The IRIS assessment applied a database UF of 3 for MC:

“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.” (p. 196)

We recommend a UF of 10 because the data-gaps involve multiple endpoints, all of which are critical for a complete and informed determination of health risks, and because available data indicates the potential for adverse effects for each endpoint. **EPA’s final risk evaluation should apply this UF in determining the benchmark MOE for MC’s non-cancer chronic effects.⁷⁷ With this adjustment and the higher UFs discussed above, the benchmark MOE for these effects would be 1000.**

E. EPA’s Final Evaluation Is Incomplete and Inadequate to Comply with TSCA In the Absence of Sufficient Data to Address Whether All Endpoints Present an Unreasonable Risk of Injury

EPA’s decision not to develop risk estimates for reproductive/development effects, developmental neurotoxicity, immunotoxicity and endocrine effects is effectively a recognition that it cannot make unreasonable risk determinations under TSCA section 6(b) for these endpoints using currently available data. Yet EPA’s obligation under TSCA is to address all conditions of use, hazards and routes of exposure in its risk evaluations. Where data-gaps prevent EPA from meeting this obligation, the Agency must obtain and assess the information necessary to determine whether health effects that are now poorly characterized present unreasonable risks of injury. The proper time to take these steps is **before** EPA initiates a risk evaluation. Section 26(k) of TSCA directs EPA to base evaluations on “reasonably available” information. The preamble to EPA’s risk evaluation framework rule underscores that information that either exists or “can be obtained through testing” is “reasonably available” and that the Agency may be obligated to require “data [to be] generated in response to EPA data gathering, including testing, authorities.”⁷⁸ For MC, however, EPA failed to use these authorities despite identifying the absence of data for critical endpoints in its 2011 IRIS assessment and 2014 Work Plan risk assessment. Any risk evaluation that EPA now finalizes without sufficient data for all endpoints would be incomplete and inadequate to comply with TSCA’s requirement to determine the unreasonable risk of injury presented by a substance as a whole. **Thus, EPA must act**

⁷⁶ Id. at 4-45.

⁷⁷ Since EPA concludes that available data for these endpoints is inadequate, it cannot rule out the possibility that MC’s immunotoxicity or developmental neurotoxicity would produce acute as well as chronic effects. For example, according to the draft evaluation, “immunosuppressive effects were observed in rats after acute exposure to 100 ppm, a lower air concentration than the levels associated with CNS effects observed in human studies.” (p. 224) To account for the possibility that these effects would be confirmed upon further testing, EPA should apply an additional 10X UF in calculating the benchmark MOE for acute effects.

⁷⁸ 82 Fed. Reg. 33726, 33732 (July 20, 2017).

expeditiously to require the necessary testing under section 4 and make an unreasonable risk evaluation for the health effects it is now unable to address.

VI. EPA's Unreasonable Risk Determinations for Workers Should Not Assume They Will be Protected by PPE

As in previous risk evaluations, EPA proposes to determine that MC's risks to workers are not unreasonable where the assumed use of Personal Protective Equipment (PPE) would reduce exposures to "acceptable" levels even though the risks would be unreasonable in the absence of PPE. The impact of this approach on EPA's risk determinations is far-reaching.

For example, EPA calculates cancer risks above its "benchmark" of 1×10^{-4} for several workplace exposure scenarios in the absence of respirators and gloves but then determines that use of PPE would lower the risk below the benchmark. If finalized, EPA's determinations of no unreasonable risk would mean that these workers receive no protection against cancer risk under section 6(a) of TSCA. EPA uses the same approach in assessing non-cancer risks to workers. EPA determines whether the Margin of Exposure (MOE) during worker exposure scenarios is greater than a so-called "benchmark" MOE, which purports to provide "adequate protection" against adverse effects. These evaluations find that numerous worker categories have highly unprotective MOEs in the absence of PPE but would be adequately protected if PPE is used. As a result, workers at risk of serious acute and non-cancer chronic effects (including death and severe incapacitation) would receive no protection under section 6(a) based on the unrealistic "expectation" that use of PPE would prevent harm.

However, as EPA's draft evaluations recognize and SACC has repeatedly underscored, this approach is not grounded in data, departs from established workplace protection policy and is contrary to the realities of worker exposure to unsafe chemicals.

A. EPA Acknowledges the Absence of Real World Evidence that Workers Consistently Wear Respirators and Gloves

For MC and previous chemicals it has evaluated, EPA assumes that "workers and occupational non-users wear respirators for the entire duration of the work activity throughout their career" and "are properly trained and fitted on respirator use." According to EPA, "similar assumptions apply to the use of gloves and their expected elimination of any dermal exposure."⁷⁹ However, EPA has repeatedly acknowledged that it has no real-world evidence to support these assumptions. Thus, in the MC draft evaluation, it admits 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)

⁷⁹ Draft Risk Evaluation for HBCD, June 2019, available at https://www.epa.gov/sites/production/files/2019-07/documents/hbcd_draft_risk_evaluation_062719_hero_link_0.pdf, at 381.

The 1-BP draft risk evaluation⁸⁰ similarly acknowledges that “[f]ew literature sources indicate the use of respirators in 1-BP conditions of use” (p. 57). Along the same lines, the 1,4-dioxane evaluation⁸¹ recognizes that “[t]he use of a respirator would not necessarily resolve inhalation exposures since it cannot be assumed that employers have or will implement comprehensive respiratory protection programs for their employees” (p. 53). It adds that gloves provide effective protection only “if proven impervious to the hazardous chemical, and if worn on clean hands and replaced when contaminated or compromised.” (p. 180).

Indeed, EPA has previously rejected reliance on respirators to reduce exposure to MC. In its January 2017 proposed ban on MC paint removers, EPA acknowledged that “not all workers may be able to wear respirators . . . Individuals with impaired lung function due to asthma, emphysema, or chronic obstructive pulmonary disease, for example, may be physically unable to wear a respirator.”⁸² EPA further observed that “individuals with facial hair, like beards or sideburns that interfere with a proper face-to-respirator seal, cannot wear tight fitting respirators,” and “respirators may also present communication problems, vision problems, worker fatigue, and reduced work efficiency.”⁸³ These considerations apply with special force to the many small facilities where MC is used and processed and where basic worker protection programs are often lacking.

EPA’s views in 2017 were informed by consultation with OSHA. In a 2016 letter to EPA, the Assistant Secretary in charge of OSHA wrote that respirators are the “least satisfactory approach to exposure control,” explaining that:

“ . . . 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.”⁸⁴

Effective use of PPE requires clear and understandable hazard warnings and directions for safe use together with adequate employee training and oversight. Yet based on numerous studies, EPA has concluded that “consumers and professionals do not consistently pay attention to labels for hazardous substances; consumers, particularly those with lower literacy levels, often do not understand label information; consumers and professional users often base a decision to follow label information on previous experience

⁸⁰ https://www.epa.gov/sites/production/files/2019-08/documents/01.1-bp_draft_risk_evaluation_hero_links_external.pdf.

⁸¹ https://www.epa.gov/sites/production/files/2019-06/documents/1_14-dioxane_draft_risk_evaluation_06-27-2019.pdf

⁸² 82 Fed. Reg. 7479.

⁸³ *Id.*

⁸⁴ 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), found at <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2014-0650-0041>

and perceptions of risk; [and] even if consumers and professional users have noticed, read, understood, and believed the information on a hazardous chemical product label, they may not be motivated to follow the label information, instructions, or warnings.” Id. EPA has also noted that label warnings and directives will only be effective if the “employer provides appropriate PPE and an adequate respiratory protection program.”⁸⁵

B. SACC Has Consistently Questioned EPA’s Assumption of Universal PPE Use

In each of its reviews of draft evaluations, the SACC has repeatedly raised concerns about EPA’s undue over-reliance on PPE for determinations of unreasonable risk. In its report on the PV29 draft, the SACC noted that “the analysis in the Evaluation does not discuss or account for the fact that downstream commercial users may be oblivious to chemical risks and lack even rudimentary industrial hygiene measures.”⁸⁶ Similarly, in reviewing the 1,4-dioxane evaluation, the SACC concluded that the “consensus of the Committee believes that PPE may not be consistently and properly worn, as EPA assumed”⁸⁷ and noted that “[g]love use should not always be assumed to be protective” and, if worn improperly, gloves “could actually lead to higher exposures.”⁸⁸ The SACC emphasized that, “[b]ecause respirators are inherently uncomfortable and potentially unreliable for long-term use, the use of respirators for more than relatively short terms is not considered appropriate in typical industrial hygiene practice.” As it concluded, “8-hour use of PPE should not be used in the risk characterization of inhaled 1,4-Dioxane. Risk estimates should be presented without the use of PPE as reasonable worst case.”⁸⁹

In the case of HBCD, the SACC noted that, “it was unreasonable to assume workers would wear PPE for entire 8-hour shifts due to underlying medical conditions, facial hair, discomfort, and other issues” and added that:⁹⁰

“[M]any members of the Committee believed EPA should place more emphasis on the limited likelihood that respiratory protection will be adopted without specific occupational exposure guidelines for HBCD . . . Dust exposures in the construction trades (especially residential

⁸⁵ 82 Fed. Reg. at 7473-4.

⁸⁶ SACC Report on PV29 at 37.

⁸⁷ SACC Report on 1,4-dioxane and HBCD, at 86. These “heighted exposures” could occur as a result of “contamination of the interior of the glove” (if workers were not properly trained in glove use and replacement) or by “acting as a reservoir” for contaminants (if the gloves were not impermeable). Despite acknowledging that protection varies greatly with different glove materials, how well they are maintained and how often they are replaced (pp. 594-597), EPA uses uniform default glove protection factors (PFs) in its evaluation of risks from dermal exposure, with the caveat (p.111) that “EPA has not found information that would indicate specific activity training (e.g., procedure for glove removal and disposal) for tasks where dermal exposure can be expected to occur in a majority of sites in industrial only OESs, so the PF of 20 would usually not be expected to be achieved.” EPA’s dermal exposure scenarios also make no allowance for the possibility of occlusion (greater penetration of the skin where contaminants build up inside the glove because it is permeable), which would result in *greater* dermal exposure than in the “no glove” scenario. The Supplemental Information on Releases and Occupational Exposure Assessment document accompanying the risk evaluation calculated significantly greater dermal exposure from glove use in occluded scenarios, but these findings are not reflected in the dermal exposure scenarios on which EPA bases its actual risk determinations. EPA, *Draft Risk Evaluation for Methylene Chloride (Dichloromethane, DCM)*, DCM Supplemental File: *Supplemental Information on Releases and Occupational Exposure Assessment*, available at https://www.epa.gov/sites/production/files/2019-10/documents/16_draft_supplemental_information_on_releases_and_occupational_exposure_assessment_public.pdf

⁸⁸ SACC Report on 1,4-dioxane and HBCD, at 55.

⁸⁹ Id. at 53.

⁹⁰ Id at 118.

construction) continue to represent an occupational health concern because of the many small-to-medium size operators and the use of temporary (and, not infrequently, undocumented) workers. Workers in these small-to-medium enterprises may not be likely to adopt personal protective equipment (PPE) controls, so EPA's characterization of reasonable risk relying on use of PPE is not sufficiently supported by the practical realities of many workplaces."

The recent SACC report on 1-BP provides further amplification of these concerns.⁹¹

"The DRE document utilizes respirator protection factor (APF) values and assumes that respirators will be used by workers. The Committee observed that while this may be accurate for larger professional organizations with resources, awareness, and knowledge, it is very likely that smaller establishments and family owned businesses (e.g., dry cleaners) will not likely use or properly utilize personal protective equipment (PPE). One Committee member highlighted the Blando et al., 2010 article, where dry cleaners did not use PPE or if a respirator was available, it was not the properly assigned respirator. The CDC MMWR study from 2008 (CDC, 2008) demonstrated that the dry cleaning index case and the case from the wave solder room in Pennsylvania did not properly operate its PPE. The wave solder case did not use respiratory protection and had a non-working cooling coil at the top of the open top batch degreaser. These experiences documented in the published papers demonstrate the difficulty of relying on PPE use for employee protection.

One member noted that the Committee has now received public testimony from two former highly distinguished Occupational Safety and Health Administration (OSHA) administrators expressing concerns regarding EPA's reliance upon non-regulatory guidance and PPE to reduce risks to reasonable levels. Persons familiar with PPE use realize that nominal protection factors may not be achieved in actual practice. The most recent of these comments also noted that compounds with high vapor pressures (such as 1-BP) may "breakthrough" cartridge type respirators in time frames much shorter than a work shift. Since respirators do not have real-time indicators of remaining capacity, respiratory protection failure is more likely for high vapor pressure compounds. 1-Bromopropane also is known to penetrate many glove types. This increases the likelihood of failure to select an appropriate glove."

The SACC concluded that EPA "[a]ssumptions about PPE use are likely unrealistic for many of the scenarios and so the determination of whether a condition of use results in an acceptable or unacceptable risk should be based on no PPE use, with the possible exception of in a manufacturing facility."⁹²

C. OSHA Regulations Do Not Support EPA Claims that Its PPE Requirements for MC Are Adequately Protective

EPA has repeatedly suggested that OSHA regulations obligate employers to implement PPE where necessary to provide effective protection against chemical risks. However, even where (as for MC) there is a chemical-specific standard in place, the primary obligation of employers is to achieve compliance through administrative and engineering controls, not PPE, and the required exposure limits may still be routinely exceeded.⁹³ Moreover, the OSHA MC standards are based on out-of-date science and both OSHA and EPA

⁹¹ SACC Report on 1-BP, at 30-31.

⁹² Id at 66.

⁹³ For example, in the preamble to its 2017 proposed paint remover rule for MC, EPA found that:

acknowledged that the 25 ppm OSHA permissible exposure limit (PEL) for methylene chloride is under-protective; in the draft risk evaluation, EPA identifies unreasonable risks at concentrations five times below the PEL. Thus, any PPE implemented to comply with the PEL would be too limited to justify a determination of no unreasonable risk.

Because of the limitations of PPE, OSHA and NIOSH manage chemical risks using the “hierarchy of controls,” under which hazard elimination, substitution, engineering and administrative controls are all prioritized over the use of PPE.⁹⁴ As explained by NIOSH, “[t]he hierarchy of controls normally leads to the implementation of inherently safer systems” because chemical regulation and substitution are “more effective and protective” than PPE. EPA’s own risk evaluation for 1,4-dioxane likewise recognizes that “[t]he most effective controls are elimination, substitution, or engineering controls [and that] “[r]espirators, and any other personal protective equipment. . . , should only be considered when process design and engineering controls cannot reduce workplace exposure to an acceptable level” (p 52). Thus, the SACC review of the HBCD evaluation stressed that “[m]any Committee members were concerned with the reliance on PPE or engineering controls to reduce risk, as that is contrary to the hierarchy of controls.”⁹⁵

EPA’s reliance on PPE to determine that unsafe MC exposures do not present unreasonable risks is not grounded in workplace realities and sound worker protection policy and thus do not adequately protect a potentially exposed or susceptible subpopulation explicitly identified in TSCA. In its final evaluation, EPA’s determinations of unreasonable risk should be based on anticipated workplace exposure levels in the absence of PPE.

VII. EPA Lacks Sufficient Exposure Data to Support Proposed Findings of No Unreasonable Risk

EPA’s evaluation of workplace risks from MC exposure is also flawed because it relies on selective and unrepresentative monitoring data and the Agency failed to use its TSCA authorities to obtain available worker exposure information from industry and state and federal agencies.

For all conditions of use, TSCA requires EPA to conduct risk evaluations based on “exposure information . . . that is reasonably available to the Administrator.”⁹⁶ EPA’s TSCA risk evaluation regulations define “reasonably available information” to include not only “information that EPA possesses” but also information that EPA “can reasonably generate, obtain, and synthesize for use in risk evaluations.”⁹⁷ EPA has substantial authority under TSCA sections 4, 8 and 11 to require the submission of existing exposure

“Many air concentrations reported and used in the risk assessment exceeded the current OSHA PEL of 25 ppm; in some industries where paint and coating removal was conducted by immersion in tanks or vats of methylene chloride, air concentrations were measured at above 7,000 milligrams per cubic meter, or 2,016 ppm. Even in industries with lower expected exposures, air concentrations frequently were reported in excess of 250 milligrams per cubic meter, or 72 ppm, such as during graffiti removal and automotive refinishing (Ref. 2).”

82 Fed. Reg. at 7477.

⁹⁴ OSH, Ctrs. for Disease Control & Prevention, updated Jan. 13, 2015, <https://www.cdc.gov/niosh/topics/hierarchy/>.

⁹⁵ SACC Report on 1,4-dioxane and HBCD, at 73.

⁹⁶ 15 U.S.C. § 2625(k).

⁹⁷ 40 C.F.R. § 702.33.

information, and to require additional monitoring or testing to fill data gaps.⁹⁸ Thus far, however, EPA has not exercised that authority in any of its draft risk evaluations. It has also failed to ask employers to share the workplace monitoring data that they are required to preserve under OSHA regulations, or asked OSHA and other state and federal agencies to provide access to the extensive exposure information in their direct possession.

The SACC was highly critical of the adequacy of the information EPA used to assess exposure in its draft risk evaluations. As stated in SACC's report on the 1,4-dioxane draft:⁹⁹

"EPA's characterization of **occupational inhalation exposure** . . . is **not** adequately supported in this draft Evaluation. The information used to evaluate worker exposure was generally lacking in its ability to present a coherent picture of this critical element of risk. Reliance on meager air monitoring data that were presented without context failed to provide the needed confidence that exposures were being reasonably evaluated." [Emphasis in original]

According to its PV29 report, SACC "considered EPA's characterization of Environmental Releases and Exposures . . . as cursory and dependent upon sweeping generalizations that are often unsubstantiated."¹⁰⁰ Regarding its occupational exposure assessment, SACC urged EPA to "clearly acknowledge that there are few data to support a confident conclusion that workers would not be exposed" to PV29 and recommended that the Agency "obtain and incorporate into the Evaluation better data and documentation from the manufacturer on conditions of use, exposures, and potential for worker exposures."¹⁰¹ SACC concluded that:¹⁰²

"Despite the compound having been in manufacture for decades, the Committee could find no basic information on the number of exposed workers and whether medical monitoring has historically been conducted. Implicit in the Evaluation is that 'absence of evidence is evidence of absence.' The Committee could not determine whether the population size or level of attentiveness were sufficient to have revealed health effects even if they exist. No evidence was provided to indicate that EPA queried other Federal or state OSHAs for information on PV29 or requested occupational hygiene or environmental release-related data from the manufacturer that are typically collected and archived."

The draft MC evaluation suffers from the deficiencies identified by SACC. For example, in his comments on the problem formulation document for the MC risk evaluation, Dr. Adam Finkel – the former Director of Health Standards Programs at OSHA – provided to EPA information on 12,152 air samples that OSHA collected on MC and which Dr. Finkel obtained from a comprehensive OSHA database pursuant to the Freedom of Information Act.¹⁰³ However, EPA references only 15 of those samples (less than 0.2%) in its draft risk evaluation, solely for the spot cleaning and fabric finishing conditions of use. EPA does not explain why the remaining data in Dr. Finkel's submission (which received a "medium" data quality score in EPA's systematic review) were not used. Nor does EPA address whether OSHA was in possession of additional MC

⁹⁸ See 15 U.S.C. §§ 2603(a), 2607(a), 2610(c).

⁹⁹ SACC Report on 1,4-dioxane and HBCD, at 21.

¹⁰⁰ SACC Report on PV29, at 16.

¹⁰¹ *Id.* at 20.

¹⁰² *Id.* at 35.

¹⁰³ See Comment by Dr. Adam M. Finkel, Docket No. EPA-HQ-OPPT-2016-0231-0536 (May 19, 2017) (Data attached as **Exhibit 1**).

monitoring data and, if so, explain why it did not contact OSHA directly to request access.¹⁰⁴ At the same time, EPA relied solely on data submitted by the Halogenated Solvents Industry Alliance (HSIA)¹⁰⁵ to determine the risks from manufacturing MC and using it as a reactant, ultimately finding no unreasonable risk to workers during these conditions of use. EPA made no effort to compare the HSIA data with the air samples submitted by Dr. Finkel or other monitoring data for the two conditions of use in the possession of OSHA or state agencies.

In finalizing the MC risk evaluation, EPA should make every effort to obtain additional workplace monitoring data from OSHA, state agencies and industry and should use all data in its possession to determine unreasonable risks to workers.

VIII. EPA Improperly Discounts Its Own Calculations of Unreasonable Risk

EPA's draft evaluation not only understates MC's risks to workers but unjustifiably downplays and mischaracterizes its own occupational risk determinations. EPA's framework for TSCA risk determinations calls for finding risks to be unreasonable where they fall below EPA's benchmark MOEs (for non-cancer effects) or above EPA's selected cancer benchmark (for carcinogenic effects). In the draft risk evaluation, however, EPA repeatedly finds that risks that meet these criteria are nonetheless reasonable, and do not warrant regulatory action under TSCA.

For example, 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). On this basis, it has determined that seven conditions of use do not present unreasonable risks for dermal exposure notwithstanding that its chronic non-cancer risk estimates (even assuming glove use) show MOEs below its benchmark (Table 4-70, pp. 346-347).

EPA's flawed risk characterizations occur most frequently with respect to so-called occupational non-users, or "ONUs," who do not regularly handle MC but are nonetheless exposed through their workplaces. The range of workers defined by EPA as ONUs – which include "supervisors, managers, engineers, and other personnel in nearby production areas" (p. 117) – is too broad to warrant a single categorization. Supervisors and managers have very different exposure patterns than skilled trade workers and other "shop floor" ONUs, yet all of them are assumed to face similar risks under EPA's categorization.

For repackaging of MC, EPA calculated ONU MOEs of 0.55 (high-end scenario) and 8.54 (central tendency scenario) for chronic exposures, compared to a benchmark MOE of 10. (p. 311). Therefore, even under the central tendency scenario, ONUs face unreasonable risks of chronic liver effects. Instead of accepting its own calculation, however, EPA states that "[i]n consideration of the uncertainties in the exposures for ONUs for this [condition of use], EPA has determined the non-cancer risks presented by chronic inhalation are not unreasonable." (p. 436) The "uncertainties" identified by EPA are that "ONU inhalation exposures are expected to be lower than inhalation exposures for workers directly handling the chemical substance" and that "[u]se of pre-PEL data may overestimate some exposures in some occupational exposure scenarios." (Id.) EPA has already accounted for the first of those uncertainties by (improperly) using central-tendency exposure estimates to calculate ONU risks; if EPA treated ONUs similarly to other workers, the risks presented by this condition of use would be nearly 20 times lower than the benchmark MOE. As for the

¹⁰⁴ MC monitoring data can be obtained directly from the OSHA Website. CHEMICAL EXPOSURE HEALTH DATA, <https://www.osha.gov/opengov/healthsamples.html>.

¹⁰⁵ Halogenated Solvents Industry Alliance Problem Formulation Comments on Methylene Chloride (Aug. 2018), <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0742-0103>.

second uncertainty, EPA has evaluated exposure data taken before and after OSHA lowered the MC PEL in 1997 and concluded that “exposure data from before the PEL (over 20 years old) are adequate for EPA’s risk evaluation purposes.”(p. 108) Having made the decision to rely upon that older data, EPA cannot discount the risk calculations that flow from that choice.

For plastic manufacturing, EPA calculated ONU margins of exposure of 8.3 from acute exposure to methylene chloride, lower than the benchmark MOE of 10. (p. 336) EPA states that “[w]hile the point estimate for the chronic non-cancer inhalation scenario estimate for ONUs indicates risk, in consideration of the uncertainties in the exposures for ONUs for this [condition of use] and the single data point for ONU exposure, EPA has determined these risks are not unreasonable.” (p. 467) For many conditions of use, however, EPA has no ONU-specific data and instead calculates ONU risks based on workers’ central-tendency exposures. Here, doing so would have resulted in an MOE of 5.4 – approximately half the benchmark MOE. (p. 336) Therefore, EPA’s typical approach *and* the ONU-specific data both support a finding of unreasonable risk.

In its final risk evaluation, EPA should adhere to its own unreasonable risk criteria and not recharacterize risks that meet these criteria as “reasonable” based on subjective and arbitrary considerations like “uncertainty.”

IX. EPA Unjustifiably Concludes that MC Does Not Present Unreasonable Environmental Risks and Fails to Address Critical Environmental Impacts

A. EPA’s Evaluation of Ecological Risk Is Flawed and Lacks Adequate Data

In its draft risk evaluation, EPA concludes that MC does not pose an unreasonable risk to the environment. However, it reaches this conclusion by excluding the studies that demonstrate the greatest environmental risk, obscuring the results of the studies that it does consider, and disregarding risk quotients more than 100 times greater than EPA’s unreasonable risk threshold.

First, EPA lacks adequate data to evaluate ecological risk. EPA does not have any studies of MC’s effects on terrestrial or sediment-dwelling species. (p. 299) EPA also has no “chronic studies that encompassed amphibian metamorphoses and adult reproductive stages of the amphibian life-cycle” (p. 204) and “no acceptable chronic exposure aquatic invertebrate studies”(p. 205). Without these data, EPA cannot fully evaluate MC’s environmental risks.

Moreover, EPA disregards the data it does have. For instance, in evaluating MC’s effects on aquatic plants, EPA selects a concentration of concern (COC) of 33.09 mg/L, based on a study of the *Chlamydomonas reinhardtii* algae species. However, in another study that EPA assigned an overall quality level of medium, “methylene chloride killed *V. steinii*,” a different algae, “at the lowest nominal concentration tested, 0.002 mg/L.” (p. 206)¹⁰⁶ Instead of using the most sensitive *V. steinii* study to select a COC, EPA states that “[t]he study supports the need for assessment factors to establish the hazard values to account for more sensitive species.” (Id.) But the 10-fold “assessment factor” applied by EPA is not nearly large enough to account for the more than 10,000-fold difference in results between those studies.

For the studies that EPA does consider, it does not select COCs based on the most sensitive species and the most sensitive endpoint, as it has done in other risk evaluations. Instead, EPA averages data across studies

¹⁰⁶ A third study, which EPA rejected as unacceptable in its systematic review, reported an EC50 of 0.98 mg/L for yet another algae species. (p. 611)

of different species and different endpoints and sets the COC based on their geometric mean. For instance, one study of MC's acute impacts on fish reported a 96-hour median lethal concentration (LC₅₀) of 108 mg/L, based on immobilization of rainbow trout (*O. mykiss*) with loss of equilibrium, melanization, narcosis, and swollen, hemorrhaging gills. (p. 205) EPA also reports that "the authors observed rainbow trout exposed to methylene chloride concentrations \geq 39 mg/L swimming at the surface, swimming erratically, and/or exhibiting melanization," indicating adverse effects below the selected LC₅₀. (Id). Another study of a different fish (*Pimephales promelas*, or fathead minnow) reported a 96-hour LC₅₀ of 502 mg/L. Instead of setting a COC that protects the most sensitive species (rainbow trout), EPA took the geometric mean of those and other studies to calculate an LC₅₀ of 242.41 mg/L. EPA relies on cross-study and cross-species averaging throughout the risk evaluation, thereby leaving the most sensitive species at risk.

EPA also discounts the results of its own calculations that indicate unreasonable environmental risks. Despite its exclusions of data and averaging of results, EPA still calculated multiple risk quotients greater than 1, the general threshold for unreasonable risk. (p. 425) For instance, of the 16 identified recycling and disposal facilities for MC, 4 had releases indicating unreasonable risks to aquatic organisms (acute RQ \geq 1 or the chronic RQ \geq 1 with 20 days or more of exceedance for the chronic COC) (p. 389 and Table 4-103). Wastewater from a Veolia Technical Solutions waste management facility in New Jersey that was shipped to Baltimore for treatment resulted in MC discharges presenting "chronic risks for multiple taxonomic groups, **with a chronic RQ for amphibians of 188.89 with 250 days of exceedance, for fish of 112.58 with 250 days of exceedance, and for aquatic invertebrates of 9.44 with 196 days of exceedance, respectively.**" (p. 389, bold added for emphasis). In other words, those discharges present chronic risks that are approximately 190 times greater than EPA deems acceptable for amphibians, 112 times greater than EPA deems acceptable for fish, and 9 times greater than EPA deems acceptable for aquatic invertebrates, lasting most of the year. However, EPA then states that "[g]iven the uncertainties in the data for the limited number of data points above the RQ, EPA does not consider these risks unreasonable." (p.32) Even if data limitations or uncertainties exist (and EPA does not specify why these projections are more limited or less reliable than EPA's other RQ calculations), that would be grounds for additional data collection and analysis, not for ignoring the underlying data or brushing aside evidence of unreasonable risk.

EPA also dismisses the evidence of harmful contamination with the following: "No acute or chronic risks to aquatic organisms were identified in ambient water; therefore, the risks identified for the five facilities mentioned above are likely localized to surface water near the facility." (p. 389). EPA provides no information on how large an area it considers to be 'ambient' or 'localized' or - most importantly - why risks to aquatic species in contaminated waters near facilities can be disregarded in determining unreasonable risks to the environment under TSCA.

SACC has been highly critical of previous risk evaluations finding the absence of unreasonable risk to the environment. For example, its report on the 1-BP evaluation concludes that "inadequate data were presented for a robust risk characterization for the environmental assessment, and the information provided did not support the conclusion of 'no unreasonable risk to the environment.'"¹⁰⁷ For 1,4-dioxane,

¹⁰⁷ SACC Report on 1-BP, at 17.

SACC concluded “that the environmental fate, exposure, and effects assessment was inadequate . . . [and that] “[m]uch more information is required to inform a robust risk assessment.”¹⁰⁸

EPA’s conclusion of no unreasonable environmental risk for MC is similarly flawed and should be eliminated from the final risk evaluation.

B. EPA Fails to Account for the Foreseeable Effects of Climate Change

In its report on the draft 1,4-dioxane risk evaluation, the SACC wrote that “[a]ir temperatures in many areas of the U.S. are 40°C for prolonged times and the magnitude of elevated temperatures as well as duration are likely to increase as a function of climate change. Temperatures of this magnitude would influence vapor pressure, water solubility, and thus Henry’s law constants, and these scenarios should be considered in exposures where inhalation is considered.”¹⁰⁹ The draft MC risk evaluation similarly fails to account for climate change in evaluating vapor pressure, water solubility, and air-water partition coefficients. Although these effects and other climate-sensitive risk evaluation inputs are chemical-specific, “in general, increasing temperature exacerbates chemical toxicity in animal models.”¹¹⁰

In addition to affecting chemicals’ physical-chemical properties, climate change is also likely to affect stream flow rates (EPA used 15–30 year old stream flow data to calculate surface water concentrations for MC), contaminant fate and transport, human sensitivity to chemical stressors, and even the use of PPE (which can be even more burdensome in higher temperature). The latest *National Climate Assessment*, an interagency effort coordinated by the United States Global Change Research Program, warns that “the assumption that current and future climate conditions will resemble the recent past is no longer valid. Observations collected around the world provide significant, clear, and compelling evidence that global average temperature is much higher, and is rising more rapidly, than anything modern civilization has experienced, with widespread and growing impacts.”¹¹¹ To the extent that specific impacts are difficult to predict, EPA may account for that uncertainty through sensitivity analyses, a broader range of temperature-related assumptions, or additional uncertainty factors. It cannot, however, ignore foreseen changes in temperatures and their impacts on the risk evaluation process.

EPA must account for the impact of climate change in its final risk evaluation.

C. EPA Fails to Address MC’s Ozone Depleting Effects

MC is an ozone-depleting substance. A 2017 study in *Nature Communications* found that rising MC emissions alone could delay the recovery of the ozone layer by 5–30 years, undermining the progress made

¹⁰⁸ SACC 1,4-Dioxane and HBCD Report, at 18.

¹⁰⁹ Id. at 42. The report also indicated that “some [SACC] members noted that [EPA] provides an estimate of the Henry’s Law constant, which reflects the distribution of 1,4-Dioxane vapors between water and air at equilibrium. However, the table does not provide the blood:air partition coefficient, which is the key parameter that an inhalation toxicologist needs to understand respiratory tract absorption.” Id. at 27. In its draft risk evaluation, EPA does not provide the blood:air partition coefficient for MC.

¹¹⁰ See Balbus, J. M., Boxall, A. B., Fenske, R. A., McKone, T. E., & Zeise, L. (2013). Implications of global climate change for the assessment and management of human health risks of chemicals in the natural environment. *Environmental Toxicology and Chemistry*, 32(1), 62-78.. doi:10.1002/etc.2046; Landis, W. G., Durda, J. L., Brooks, M. L., Chapman, P. M., Menzie, C. A., Stahl Jr, R. G., & Stauber, J. L. (2013). Ecological risk assessment in the context of global climate change. *Environmental Toxicology and Chemistry*, 32(1), 79-92.. doi:10.1002/etc.2047.

¹¹¹ U.S. Global Change Research Program, *Fourth National Climate Assessment Volume II: Impacts, Risks, and Adaptation in the United States* 36 (2017).

under the Montreal Protocol.¹¹² The National Oceanic and Atmospheric Administration (NOAA) called MC a “possible new threat to the Earth’s ozone layer.”¹¹³

EPA completely ignores these ozone-depleting effects in its draft risk evaluation. Ozone depletion presents both risks to the environment – which TSCA defines broadly to include “water, air, and land and the interrelationship which exists among and between water, air, and land and all living things”¹¹⁴ – and human health risks, through increased rates of skin cancer and cataracts.¹¹⁵ EPA previously regulated chlorofluorocarbons under TSCA precisely because they “produce a risk to human health and the environment by causing depletion of the ozone layer.”¹¹⁶ In fact, depletion of the ozone layer was one of the concerns that motivated the passage of TSCA in the 1970s.¹¹⁷

Considerable progress has been made to repair the ozone layer since then, making it all the more important for EPA to evaluate whether MC emissions will slow or reverse that progress. EPA cannot claim that MC’s ozone-depleting effects are adequately addressed by the CAA, since EPA has not controlled MC under Title VI of the Clean Air Act (which regulates stratospheric ozone pollution) and more than 2.5 million pounds of MC are emitted to the air each year, according to TRI data.¹¹⁸

EPA’s final risk evaluation must address the environmental and human health risks associated with MC’s depletion of the ozone layer.

X. EPA Must Abandon its Flawed TSCA Systematic Review Method and Apply Scientifically Valid and Peer-Reviewed Systematic Review Methodologies

Like previous evaluations, EPA is using “systematic review” criteria developed by the TSCA program¹¹⁹ to evaluate the quality of available data on MC. Our organizations have previously commented that the TSCA method represents a deeply flawed and unscientific approach to systematic review that will compromise the quality, validity and protectiveness of the 10 risk evaluations.¹²⁰ These concerns were summarized in a recent peer-reviewed commentary published in the *American Journal of Public Health*.¹²¹

¹¹² Hossaini, R., Chipperfield, M., Montzka, S. et al. (2017). The increasing threat to stratospheric ozone from dichloromethane. *Nat Commun.* 8, 15962. doi:10.1038/ncomms15962.

¹¹³ *Possible New Threat to Earth’s Ozone Layer*, NOAA Research News (June 30, 2017), <https://research.noaa.gov/article/ArtMID/587/ArticleID/130/Possible-new-threat-to-Earth’s-ozone-layer>.

¹¹⁴ 15 U.S.C. § 2602.

¹¹⁵ EPA, *Health and Environmental Effects of Ozone Layer Depletion* (Sept. 24, 2018), <https://www.epa.gov/ozone-layer-protection/health-and-environmental-effects-ozone-layer-depletion>.

¹¹⁶ Fully Halogenated Chlorofluoroalkanes, 43 Fed. Reg. 11,318, 11,318 (Mar. 17, 1978).

¹¹⁷ See S. Rep. No. 94-698, at 4 (1976) (identifying “depleti[on of] the Earth’s ozone layer which protects humans from excessive ultraviolet radiation that can cause skin cancer” as one of the “significant health and environmental dangers” to be addressed by TSCA).

¹¹⁸ See note 24 *supra*.

¹¹⁹ 83 Fed. Reg. 26998 (June 11, 2018); Application of Systematic Review in TSCA Risk Evaluations, available at https://www.epa.gov/sites/production/files/2018-06/documents/final_application_of_sr_in_tsca_05-31-18.pdf

¹²⁰ Comments of Safer Chemicals Healthy Families et al. on Application of Systematic Review in Risk Evaluations under Section 6 of the Amended Toxic Substances Control Act, August 16, 2018, Docket ID EPA-HQ-OPPT-2018-0210. We incorporate these comments by reference.

¹²¹ Singla V, Sutton P, Woodruff TW. (2019) The Environmental Protection Agency Toxic Substances Control Act Systematic Review Method May Curtail Science Used to Inform Policies, With Profound Implications for Public Health. *Am J Public Health*. doi: 10.2105/AJPH.2019.305068

“Systematic review” is a well-established approach for evaluating and integrating scientific evidence to arrive at judgments about hazard, exposure and risk. The EPA framework risk evaluation rule recognizes the need for a systematic review process in determining chemical risks under TSCA.¹²² However, the TSCA method departs radically from accepted scientific principles for systematic review adopted by the IOM,¹²³ the NTP¹²⁴ and EPA’s Integrated Risk Information System (IRIS)¹²⁵ and endorsed by the NAS¹²⁶ and other peer review bodies.

The TSCA approach applies a rigid scoring system to grade the “quality” of studies on chemicals. This system could result in many studies being arbitrarily classified as “poor” or “unacceptable” based on a small number of reporting or methodology limitations that do not negate their overall value for assessing health and environmental risks. The consequence will be that important evidence of public health impacts – particularly epidemiological studies demonstrating harm in human populations – will be either disregarded or given limited weight in risk evaluations. Other systematic review methodologies do not use numerical scoring systems for assessing study quality and the NAS recommends strongly against such scoring.

The TSCA approach also focuses on one limited aspect of systematic review – study quality – but fails to address other critical elements that the Agency itself recognizes are essential for science-based risk judgments. EPA’s July 2017 risk evaluation framework rule defines systematic review as a comprehensive, consistent and transparent process to “identify and evaluate each stream of evidence” and “to integrate evidence as necessary and appropriate based on strengths, limitations, and relevance.”¹²⁷ Yet the TSCA document lacks any protocol for these important tasks. Experts agree that a protocol for the review needs to be established in advance of individual evaluations to eliminate the potential for bias and to assure that evidence reviews are conducted using consistent, well-defined criteria. EPA’s failure to take this necessary step *before conducting risk evaluations* has severely compromised the scientific validity of the 10 initial TSCA risk evaluations.

¹²² 82 Fed. Reg. 33726, 33734 (July 20, 2017).

¹²³ Institute of Medicine. Finding What Works in Health Care. Standards for Systematic Review. Washington, D.C.: The National Academies Press.; 2011.

¹²⁴ National Toxicology Program. Handbook for Conducting a Literature-Based Health Assessment Using OHAT Approach for Systematic Review and Evidence Integration. In: U.S. Department of Health and Human Services, editor.: Office of Health Assessment and Translation, Division of National Toxicology Program, National Institute of Environmental Health Sciences; 2015.

¹²⁵ National Research Council. Review of EPA's Integrated Risk Information System (IRIS) Process. Washington, DC: National Academies Press; 2014.

¹²⁶ National Research Council. Review of EPA's Integrated Risk Information System (IRIS) Process. Washington, DC: National Academies Press; 2014; National Research Council. Review of the Environmental Protection Agency’s State-of-the-Science Evaluation of Non Monotonic Dose–Response Relationships as They Apply to Endocrine Disruptors. Washington, DC: National Academies Press; 2014; National Academies of Sciences, Engineering, and, Medicine. Application of Systematic Review Methods in an Overall Strategy for Evaluating Low-Dose Toxicity from Endocrine Active Chemicals. Washington, DC: 2017.

¹²⁷ 40 C.F.R. 704.33.

Recent draft risk evaluations have also been based on a “hierarchy of preferences,” a new concept that was not part of the original TSCA systematic review document and has likewise not been subject to peer review or public comment. The 1-BP evaluation briefly explains this approach as follows.¹²⁸

“EPA’s approach uses a hierarchy of preferences that guide decisions about what types of data/information are included for further analysis, synthesis and integration into the environmental release and occupational exposure assessments. EPA prefers using data with the highest rated quality among those in the higher level of the hierarchy of preferences (i.e. data>modeling>occupational exposure limits or release limits).”

EPA does not explain why some types of studies should receive preference over others in determining the weight of evidence for a particular endpoint and on what basis these studies should be assigned to a “higher level.” Thus, there are no objective criteria for determining which evidence to rely on and which to exclude, undermining transparency and consistency in the systematic review process and encouraging subjective judgments.

As reflected in the draft MC evaluation, EPA has also updated the TSCA data quality criteria for epidemiological studies.¹²⁹ The updated criteria make it more difficult for epidemiological studies to be scored as high quality and thus limit the weight they receive in the MC evaluation, reflecting a consistent tendency by the EPA TSCA program to downplay the value of human evidence. EPA has failed to explain or justify the updated criteria.

In its peer review of the draft risk evaluation of PV29, the EPA SACC highlighted the following areas of concern with the TSCA systematic review method:

- “The Agency rationale for developing the TSCA SR should include a comparison to other SR approaches and describe the rationale for major differences.”¹³⁰
- “The Committee discussed the need to publish peer reviewed pre-established protocols for each of the Agency’s reviews prior to performing the actual risk assessment. The protocol for PV29 was created concurrently with the review, which is contrary to best practices for systematic reviews.”¹³¹
- “The Committee noted that the TSCA SR weighted scoring system may be inappropriate if there is disagreement in the weighting of different metrics. For example, a certain study characteristic that may be a ‘fatal flaw’ would be weighted equally to other more minor elements. The Agency should provide justification for using a weighted scoring system and the rationale for the specific metrics used for differential weighting in its evaluation of studies.”¹³²

¹²⁸ Draft Risk Evaluation for 1-Bromopropane, August 2019, at 45, available at https://www.epa.gov/sites/production/files/2019-08/documents/01_1bp_draft_risk_evaluation_hero_links_external.pdf.

¹²⁹ The completed data quality evaluation for MC epi studies using the updated criteria can be found in the Supplemental File: Data Quality Evaluation of Human Health Hazard Studies – Epidemiological Studies (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. Systematic Review Supplemental File.

¹³⁰ PV29 SACC Report at 26.

¹³¹ Id. at 27.

¹³² Id. at 26-7.

- “Regarding data integration, the Committee discussed the benefits of including a more thorough and inclusive data integration discussion in the TSCA SR for PV29 ... there is a need in the Evaluation for a thorough description and outline for how all evidence and data are integrated into a final weight of evidence conclusion.”¹³³

The SACC also strongly recommended that EPA move forward with National Academy of Sciences (NAS) review of its TSCA systematic review method – a commitment on which EPA dragged its feet for months until recently signing an agreement with NAS.¹³⁴

These concerns were forcefully underscored in the SACC review of the 1,4-dioxane risk evaluation:¹³⁵

“Committee members did not find the systematic review to be a transparent and objective method to gather the relevant scientific information, score its quality, and integrate the information. Several Committee members brought up examples of references that were not in the systematic review bibliography and/or not considered in the Data Quality evaluation step, but which were used at different stages in the Evaluation. Several Committee members found that it was difficult to determine whether the relevant information was properly evaluated and considered in the Evaluation.”

The SACC “noted problems with both the systematic review design and consistent implementation of its protocols,” elaborating that:¹³⁶

“Signs that the systematic review design has issues include the need for ‘backward reference searching’ or ‘targeted supplemental searches,’ which shouldn’t be required if the initial search finds all the relevant references. Similarly, the Committee noted a high fraction of studies where the initial quality score was later changed, indicating that the data quality evaluation protocol is not clearly defined and possibly inconsistently implemented by different reviewers. The automated gray literature search found mostly several off-topic documents and also missed other useful documents.”

The SACC report further indicated that “[s]everal Committee members recommended simplifying the scoring system or adopting an existing peer-reviewed method, such as the method used by the National Toxicology Program’s Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR).”¹³⁷

The SACC report on the 1-BP draft evaluation noted “challenges in following how the studies identified for data integration during the SR were applied throughout the draft evaluation.”¹³⁸ It elaborated that:

“Members noted that studies identified for data integration were difficult to match with references cited in the bibliography. There are occasional cases where key references and data used in the risk characterization did not go through data quality evaluation (DQE) at all, although that is the Committee’s expectation. Members noted that there were multiple instances where the explanation of why papers rated highly in the DQE but not used in the draft risk evaluation was missing or incomplete. The Committee identified at least one instance where a study was rated low under data

¹³³ Id. at 27.

¹³⁴ <https://www8.nationalacademies.org/pa/projectview.aspx?key=51889>

¹³⁵ 1,4-Dioxane and HBCD SACC Report, at 30.

¹³⁶ Id. at 31.

¹³⁷ Id.

¹³⁸ SACC Report on 1-BP, at 12.

quality evaluation based on a reference not being available. Committee members were able to readily obtain that reference in the public literature with a simple search. Examples such as this suggest that there is continued room for improvement in EPA's internal processes for SR. The Committee also identified several areas where corrections or additional clarification is needed."

Thus far, the serious issues and concerns raised by SACC have not been addressed by EPA in its most recent draft evaluations. At a minimum, EPA's final risk evaluations must respond fully to SACC's comments and implement its recommendations.

The SACC and others have raised more far-reaching concerns about the scientific validity and underpinnings of the TSCA systematic review method. Belatedly, EPA is finally following through on its commitment to commission an NAS review of its method, a course that the SACC has repeatedly recommended and to which EPA agreed nearly a year ago. While the NAS review is progressing, we believe EPA should abandon the TSCA systematic review method immediately and not use it in developing final risk evaluations. Instead, it must adopt one of the recognized systematic review methodologies developed by IOM, NTP and EPA's IRIS program and endorsed by the NAS and other peer review bodies.

Conclusion

We appreciate this opportunity to comment on the draft MC risk evaluation.

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