**AMERICAN CHEMISTRY COUNCIL COMMENTS**

**ON THE DRAFT RISK EVALUATION**

**FOR METHYLENE CHLORIDE**

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## TABLE OF CONTENTS

**Executive Summary**

ACC commends EPA's efforts in its draft TSCA risk evaluation of methylene chloride but also offers some recommendations for the Agency to consider as it finalizes this risk evaluation. The aim of ACC's comments is to help EPA ensure that its final risk evaluation meets the TSCA statutory and regulatory requirements that it be based on best available science and weight of the scientific evidence. ACC's comments also seek to ensure that the basis of the Agency's risk determinations for methylene chloride's conditions of use are clear and transparent. ACC also notes the importance of the technical comments provided in writing and verbally to the EPA's SACC on methylene chloride.

In these comments, ACC recommends that EPA:

- Fully evaluate and discuss the plausibility of the **alternative cancer mode of action (MOA)** for methylene chloride and weigh the scientific evidence of this alternative approach as part of the risk characterization. To aid in this process, EPA should utilize an established framework to organize evidence for MOA based on side-by-side weight of evidence comparison of alternative plausible MOAs.
- **Use tiered approaches** to exposure modeling to verify model outputs and ensure they represent exposure levels in line with real-world conditions.
- **Clarify its assumptions related to environmental release scenarios,** including how volatilization and dilution are considered in the analyses.
- **Provide more information** in this and other risk evaluations **about how EPA determines whether existing EPA regulations are adequate to address risks** associated with the chemical under its conditions of use. EPA should also be more transparent about its consultation and coordination with OSHA when the Agency addresses worker exposures in the risk evaluations.
- **Increase transparency in systematic review approaches**. This includes providing more detail and specificity on: its approach to study quality evaluation of *in vitro* and mechanistic information; and the data integration phase of the TSCA systematic review in the final methylene chloride risk evaluation, in particular, integration of epidemiological evidence. In addition, while EPA has recognized that the data integration phase of the TSCA systematic review approach is still being developed, EPA should begin now to build out its general approach to data integration in separate guidance.
- **Clearly present** the supporting data, information, and analyses underlying both the risk characterization and the risk determination. EPA should employ a consistent format for making clearer how EPA's risk characterizations support its risk determinations.

## Introduction

In each TSCA risk evaluation, EPA must meet relevant statutory and regulatory requirements. The statutory requirements most relevant to risk evaluations are TSCA Sections 6(b)(4)(A) and 6(b)(4)(F)[1], and the scientific standards of Section 26(h) and 26(i).[2] The applicable regulatory requirements are addressed in EPA's final Procedures for Chemical Risk Evaluation under the Amended Toxic Substances Control Act.[3] (Risk Evaluation Rule).

The TSCA statutory requirements address the general purpose of risk evaluations, certain general requirements for the risk evaluations, and the science standards that the risk evaluations must be based upon.

The Risk Evaluation Rule reflects TSCA's general statutory requirements but includes more specific requirements. These include: definitions at 40 CFR §702.33; detailed requirements of the risk evaluation at 40 CFR §703.41 on: the scope of the risk evaluation, (including conceptual plan and analysis plan); the hazard assessment; and the exposure assessment; the risk characterization considerations at 40 CFR §702.43; and the unreasonable risk determination at 40 CFR §702.47. Throughout each of these regulatory sections, the factors EPA must consider in a risk evaluation and required documentation of certain requirements are prescribed.

Each TSCA risk evaluation must satisfy all the elements of TSCA Section 6(b)(4)(A)'s statement on the general purpose of risk evaluations: "to determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant in the risk evaluation by the Administrator, under the conditions of use."

In addition, each risk evaluation must meet TSCA Section 6(b)(4)(F)'s general requirements for EPA to meet in conducting a risk evaluation…Specifically, ***EPA shall***:

- ***Integrate and assess available information on hazards and exposures*** for the conditions of use of the chemical substance (including information about specific risks of injury to health or environment and information on potentially exposed or susceptible subpopulations identified as relevant by EPA)
- ***Describe whether aggregate or sentinel exposure*** to a chemical under the conditions of use were considered, and the basis for that consideration
- ***Not consider*** costs or other non-risk factors
- ***Take into account, where relevant, the likely duration, intensity, frequency, and number of exposures*** under the conditions of use of the chemical; and
- ***Describe the weight of the scientific evidence*** for the identified hazard and exposure.

TSCA Section 26 also includes science-based requirements that EPA must meet. Specifically, TSCA Section 26 (i) mandates that EPA make decisions under Sections 4, 5 and 6 of TSCA "***based on the weight of the scientific evidence.***" TSCA Section 26(h) mandates that in carrying

[1] 15 U.S.C. 2605(b)(4)(A) and 15 U.S.C. 2605(b)(4)(F)
[2] 15 U.S.C. 2625(h) and 15 U.S.C. 2625(i)
[3] 82 Fed. Reg. 33726, July 20, 2017. Codified at 40 C.F.R. Part 702, Subpart B, Sections 702.31-702.51

out Sections 4, 5 and 6, "to the extent that the Administrator makes a decision based on science, the Administrator shall use scientific information, technical procedures, measures, methods, protocols, methodologies, or models employed in a manner consistent with the ***best available science***.

The statutory and regulatory requirements form the "framework" for review of this and future TSCA draft risk evaluations. ACC commends EPA's efforts, and we offer recommendations for EPA to consider in the final risk evaluation of methylene chloride (MC).[4] ACC's particular objective in these comments is to ensure that EPA meets the statutory and regulatory requirements for basing its final risk evaluation of MC on "best available science" and "weight of the scientific evidence" in a clear manner.

## I. Human Health Hazard Assessment

### A. EPA's Cancer Mode of Action Approach and Discussion (Section 3.2.3.2.1) Should Be Revisited with Full Consideration of Alternative Plausible MOAs.

The risk evaluation for MC addresses the potential mutagenic mode of action (MOA) for cancer, however it does not fully evaluate, discuss, or weigh the mechanistic evidence for alternative, biologically plausible MOAs. As a result, the potential risks associated not only with the default option, but also the potential risks from biologically plausible alternatives (as required by the Risk Evaluation Rule[5]) have not been fully and transparently characterized. ACC recommends that EPA revisit the MOA approach by considering alternatives with biological support in the final risk evaluation.

A recent study on MC has proposed a non-mutagenic, threshold MOA for carcinogenicity in mice involving CO production and formation of COHb as key events, thus demonstrating a biologically-plausible alternative to a genotoxic MOA resulting from glutathione pathway metabolites.[6] However, this paper was not referenced in the risk evaluation, and EPA did not thoroughly consider and present this alternative MOA. EPA should consider this peer-reviewed, scientific analysis, as it meets the Agency's definition of best available science. Accordingly, EPA should acknowledge this alternative MOA and present the weight of evidence supporting a non-mutagenic, threshold MOA for tumor formation resulting from exposure to MC in laboratory animals.[7]

The language and spirit of the 2016 amendments to TSCA and the Risk Evaluation Rule encourage the Agency to consider alternatives to default assumptions in order to reflect the best

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[4] U.S. EPA, 2019, Draft Risk Evaluation for Methylene Chloride CASRN:75-09-2. EPA Document# EPA-740-R1-8010. Office of Chemical Safety and Pollution Prevention, U.S. Environmental Protection Agency: Washington, D.C.

[5] 40 CFR 702.41(c)(5)(ii); 40 CFR 702. 43(a)(5); 40 CFR 702.43(b)(3);

[6] Andersen, M.E., Black, M.B., Pendse, S., Clewell, H.J. III, McMullen, P.D., Bus, J., Pottenger, L. and Campbell, J.L. (2017). Combining transcriptomics and PBPK modeling of carboxyhemoglobin to assess modes-of-action for dichloromethane in mouse lung and liver: evidence for a primary role of hypoxia in tissue responses. Toxicol. App. Pharmacol., 332,149-158.

[7] Further information regarding this MOA is discussed in the comments from Mel Andersen to the SACC, Docket ID: EPA-HQ-OPPT-2019-0437-0034.

available science. Recognizing and acting on advances in scientific knowledge and the best available, most relevant data and dose-response models will strengthen the scientific foundation of the risk evaluation. The review and application of MOA hypotheses and human relevance are addressed in EPA's 2005 cancer risk assessment guidelines.[8] The guidelines state:

> When there are alternative procedures having significant biological support, the Agency encourages assessments to be performed using these alternative procedures, if feasible, in order to shed light on the uncertainties in the assessment, recognizing that the Agency may decide to give greater weight to one set of procedures than another in a specific assessment or management decision.[9]

The Agency's Cancer Guidelines also clearly state:

> If critical analysis of agent-specific information is consistent with one or more biologically based models as well as with the default option, **the alternative models and the default option are both carried through the assessment and characterized for the risk manager** [emphasis added]. In this case, the default model not only fits the data, but also serves as a benchmark for comparison with other analyses. This case also highlights the importance of extensive experimentation to support a conclusion about mode of action, including addressing the issue of whether alternative modes of action are also plausible.[10]

EPA's Cancer Guidelines emphasize the importance of considering alternative MOAs and expressly recommend that alternatives to the default having substantial biological support be carried through the assessment and resulting risk calculations be characterized and presented to the risk manager. In its TSCA risk evaluations, EPA should more clearly and transparently present biologically robust, MOA assessments where the weight of the evidence is integrated fully. Ultimately, EPA should carry any biologically plausible alternative MOAs and the default MOA option through the entire assessment and present all risk calculations in the risk characterization section.

### B. EPA Should Utilize an Established Framework to Organize Evidence for MOA and to Support Decisions Based on Side-by-Side Weight of Evidence Comparison of Alternative Plausible MOAs

EPA could strengthen its evaluation of the plausible MOA(s) for the potential carcinogenicity of MC using more structured methods to organize, integrate, and communicate its findings on mutagenicity (among other endpoints). There are several existing organizational methods and frameworks that better facilitate evidence integration, which EPA should consider using in its TSCA risk evaluations. Other approaches can streamline procedures and where possible, include quantitative information. For example, EPA could consider the use of adverse outcome pathways (AOPs) to organize potential mechanisms into models that describe how exposure to MC might cause cancer (e.g., using the approach of the OECD Adverse Outcome Pathway

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[8] US EPA, Guidelines for Carcinogen Risk Assessment, Risk Assessment Forum, US Environmental Protection Agency, Washington, DC, EPA/630/P-03/001F, March 2005 (Cancer Guidelines).
[9] *Id.*, at 1-8.
[10] *Id.*, at 1-9.

(AOP) methodology).[11] EPA could also consider using the MOA approach initially championed by the World Health Organization (WHO)/International Programme on Chemical Safety (IPCS), which is utilized by other EPA program offices. [12,13] EPA could also apply MOA confidence scores, as described by Becker et al. (2017).[14] Further details on approaches EPA should consider are provided below.

1. **The WHO/IPCS MOA Framework**

EPA's Office of Pesticide Programs (OPP) has considerable experience with application of MOA frameworks and has adopted the WHO/IPCS MOA framework for organizing, evaluating, and integrating hazard and dose response information.[15] The MOA framework can be used to illustrate the key events in a known toxicity pathway to address whether a reported statistically significant response is consistent with what is expected based upon knowledge of the biological responses comprising the pathway. It should be noted that even if early biological responses/perturbations are detected, these observations are not necessarily adverse or precursors to adverse effects in living organisms because of adaptive or homeostatic mechanisms.[16] To reliably predict toxicity, key events need to be bridged to adversity with a clear understanding of dose response/temporal key event relationships. Standard MOA templates for both cancer and non-cancer endpoints, such as the dose/temporal concordance and species concordance templates, can be utilized. These types of templates have been incorporated by the European Chemicals Agency (ECHA) in implementing Europe's Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) program.[17]

2. **Weight of Evidence Confidence Scores**

Because the scientific justification for assessing human relevance and selecting dose-response extrapolation methods for quantifying potential human health risks is highly dependent upon the determination of the likely operative MOA, a systematic and explicit approach must be uniformly implemented to compare potentially relevant MOAs. One method for doing this involves deriving WOE confidence scores based on the IPCS framework and Bradford Hill causation criteria. This enables a side-by-side comparison of numerical WOE confidence scores for different hypothesized MOAs. This method allows for effective identification of the most

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[11] https://www.oecd.org/chemicalsafety/testing/adverse-outcome-pathways-molecular-screening-and-toxicogenomics.htm

[12] Boobis, AR, et al, 2006. IPCS Framework for Analyzing the Relevance of a Cancer Mode of Action for Humans. Critical Reviews in Toxicology, 36:10, 781-792, DOI: 10.1080/10408440600977677; Meek, ME, et al, 2014. New developments in the evolution and application of the WHO/IPCS framework on mode of action/species concordance analysis. J. Appl. Toxicol, 34(1): 1-18. http://dx.doi.org/10.1002/jat.2949.

[13] Boobis, AR, et al, 2006. IPCS Framework for Analyzing the Relevance of a Cancer Mode of Action for Humans. Critical Reviews in Toxicology, 36:10, 781-792, DOI: 10.1080/10408440600977677; Meek, ME, et al, 2014. New developments in the evolution and application of the WHO/IPCS framework on mode of action/species concordance analysis. J. Appl. Toxicol, 34(1): 1-18. http://dx.doi.org/10.1002/jat.2949.

[14] Becker, RA, et al. 2017. Quantitative weight of evidence to assess confidence in potential modes of action. Regul. Toxicol. Pharmacol.86: 205-220. doi: https://doi.org/10.1016/j.yrtph.2017.02.017.

[15] https://www.who.int/ipcs/methods/harmonization/areas/cancer/en/;

[16] Becker, RA, et al. 2017. Quantitative weight of evidence to assess confidence in potential modes of action. Regul. Toxicol. Pharmacol.86: 205-220. doi: https://doi.org/10.1016/j.yrtph.2017.02.017.

[17] https://echa.europa.eu/documents/10162/22315482/whoipcs_moa_template_withinstructions.docx/b98feba9-a37c-489d-94b0-dd5fbb2ed468

likely MOA, thereby enhancing transparency and improving communication among risk managers and the public.[18] Furthermore, this best available science approach provides a transparent, scientifically sound justification for using the most likely operative MOA as the basis for selecting the most appropriate extrapolation method for calculating potential risks to humans from environmentally relevant exposures.

### C. EPA Should Reconsider Its Review of Epidemiological Evidence because Its Cancer Hazard Conclusions Do Not Appropriately Weigh that Evidence

Hazard and exposure information must be integrated and assessed in each risk evaluation per the TSCA statutory language and the regulatory requirements of the Risk Evaluation Rule. The MC draft risk evaluation makes some progress in the integration of data, but further work is needed in both this draft and in the general systematic review guidance. While there are various ways to integrate data, EPA must integrate information in a way that is fit-for-purpose to meet the statutory and regulatory requirements noted above.[19] EPA discusses data integration in the TSCA guidance document on systematic review, identifying this as a critical step for TSCA Risk Evaluations.[20] However, the systematic review guidance offers no specifics on EPA's approach to data integration and states that, "EPA/OPPT will provide further details about the data integration strategy along with the publication of the draft TSCA risk evaluations."

An example that illustrates how the data integration could be improved relates to the discussion of epidemiological evidence. In Section 3.2.4.2 (page 264), EPA states, "[a]lthough a number of relevant studies are available, findings were inconclusive for cancers of the liver, lung, breast, brain and CNS, and most hematopoietic cancer types, due to weaknesses of the individual studies and inconsistent results across studies. For these endpoints, the epidemiological studies provide only limited support for a relationship between methylene chloride exposure and tumor development." EPA's data quality assessment rated most of the epidemiological studies as medium to high quality; however, it discounts them as not providing evidence of a relationship, stating that the epidemiological evidence on cancer is largely "inconclusive." For example, the risk evaluation states, "Most of the human data on lung cancer and methylene chloride exposure are not conclusive and most do not show an association with methylene chloride (Table 3-8)."

However, the draft risk evaluation highlighted three recent studies that observed positive associations between MC and B-cell non-Hodgkin lymphomas (Seidler et al., 2007; Barry et al., 2011; and Miligi et al., 2006). These case control studies were classified as high quality, but Barry et al. (2011) was the only one that reported a statistically significant result. EPA states that "firm" conclusions could not be made regarding B-cell lymphoma, and again cited inconclusive results for hematpoietic cancers in general. Ultimately, however, EPA concludes that MC is considered "likely to be carcinogenic to humans" based on sufficient evidence in

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[18] Becker, RA, et al. 2017. Quantitative weight of evidence to assess confidence in potential modes of action. Regul. Toxicol. Pharmacol.86: 205-220. doi: https://doi.org/10.1016/j.yrtph.2017.02.017.

[19] In particular, 40 CFR 702.33 (definitions of best available science and weight of the scientific evidence) and 40 CFR 702.41(a)(4) (regarding use of best available science and weight of the scientific evidence).

[20] Application of Systematic Review in TSCA Risk Evaluations, May 2018, EPA Document# EPA- 740-P1-8001. U.S. Environmental Protection Agency Office of Chemical Safety and Pollution Prevention.

animals and "limited supporting evidence in humans" [emphasis added]. This conclusion is not supported by the evidence.

While in experimental studies, mice exposed to high concentrations of methylene chloride via inhalation for two years developed liver and lung tumors, similarly exposed rats developed only benign mammary tumors, and hamsters developed no tumors. The inter-species inconsistencies in carcinogenic effect have been attributed to dosimetry and metabolic differences across species.[21,22,23] *In vitro* evidence indicates that MC is mutagenic in bacteria, but findings *in vivo* remain inconsistent, with no evidence of DNA adduct formation or gene mutations *in vivo*; as discussed in detail above, recent analyses support a non-mutagenic MOA.[18] The species inconsistencies were explicitly called out and evaluated by ACGIH in 2001 when deriving their threshold limit value for workers. ACGIH ultimately concluded that the weight of the evidence, particularly when considering the exposure-response information from the Kodak epidemiological studies, did not demonstrate that MC is carcinogenic in humans.[24]

It appears as though, despite the generally null findings in studies rated as "medium" and "high" quality, the draft risk evaluation suggests that the available epidemiological studies simply failed to detect associations owing to "inherent limitations" of epidemiological studies. Given that the studies were relatively well conducted, however, this argument is unfounded. Further, several of the general limitations discussed were not limitations of the MC cancer epidemiology. For example, EPA notes the possibility of low numbers of deaths or cases reported for some cancers. For multiple cancers, including lung cancer, adequate numbers were available to evaluate whether there was increased cancer risk. On the other hand, the few positive associations reported (e.g., the studies reporting increased risk of diffuse large B-cell lymphoma and multiple myeloma, respectively), were based on small numbers, and could be chance false-positive findings.

The purpose of a study quality tool is to determine the level of confidence one can place in a body of evidence for the purposes of evidence integration; relatively well-conducted studies that do not "fit" with the other lines of evidence should not be dismissed as inconclusive.

EPA should consider revising its review and synthesis of the epidemiological evidence to more fully incorporate the strengths and weaknesses of the epidemiological studies, and integrate these studies with the available animal and mechanistic evidence to support conclusions regarding carcinogenic hazard.

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[21] Andersen, M.E., Black, M.B., Pendse, S., Clewell, H.J. III, McMullen, P.D., Bus, J., Pottenger, L. and Campbell, J.L. (2017). Combining transcriptomics and PBPK modeling of carboxyhemoglobin to assess modes-of-action for dichloromethane in mouse lung and liver: evidence for a primary role of hypoxia in tissue responses. Toxicol. App. Pharmacol., 332,149-158.
[22] Andersen M.E., Clewell H.J. 3rd, Gargas M.L., Smith F.A., Reitz R.H. (1987). Physiologically based pharmacokinetics and the risk assessment process for methylene chloride. Toxicol Appl Pharmacol., 87(2), 185-205.
[23] Green, T. (1997). Methylene chloride induced mouse liver and lung tumours: An overview of the role of mechanistic studies in human safety assessment. Hum Exp Toxicol 16, 3-13.
[24] ACGIH 2001. TLV Documentation: Methylene Chloride.

### D. EPA Should Expand the Discussion of the Uncertainty Associated with the Route-to-Route Extrapolation for Dermal Hazard Evaluation

In the MC draft risk evaluation EPA has performed a route-to-route extrapolation to evaluate dermal exposures. However, Section 3.2.1 (page 217) states, "[n]o acceptable toxicological data are available by the dermal route. Furthermore, dermal absorption data and physiologically-based pharmacokinetic/pharmacodynamic (PBPK/PD) models that would facilitate route-to-route extrapolation to the dermal route have not been identified for methylene chloride. Therefore, inhalation PODs were extrapolated for use via the dermal route using models that incorporate volatilization, penetration and absorption…" Further, in Section 3.2.5.2.3 (Page 282) EPA notes, "there is uncertainty regarding the likelihood that dermal exposure will result in lung cancer, but because humans may experience different cancers than rodents, EPA has assumed that the slope factor of the combined tumor types can be considered generally representative of the potential for cancers of other types and that this is relevant to model *via* the dermal route." Due to the lack of sufficient dermal toxicokinetic and effect data this route-to-route extrapolation is highly uncertain and would benefit from more discussion. Several points to clarify in the hazard assessment section could include:

- **Precedent:** EPA should identify appropriate guidance and examples that illustrate inhalation-to-dermal extrapolation is an appropriate default approach. Since data are lacking for MC, are there similar volatile compounds where this method has been applied?
- **Toxicokinetics**: A discussion of toxicokinetic factors that influence the route-to-route extrapolation (*e.g.*, absorption across lung or skin) should be included and relevant data should be cited.[25] For example, a comparison of external and internal doses for each route should be included to determine if the inhalation PODs should be adjusted for absorption to estimate an appropriate dermal POD.
- **Route Dosimetry**: Since MC is a highly volatile chemical, dermal exposure would not be constant (*i.e.*, concentrations would be variable and decreasing as a portion of the dose volatilizes), while the inhalation exposure from animal studies is maintained at a relatively constant concentration. Thus, a route-to-route extrapolation from inhalation exposure to dermal exposures is likely to result in an extremely conservative estimate of potency.
- **Irritation Hazard**: EPA acknowledges that there is an irritation/burn hazard with MC (Section 3.2.3.1.6). Irritation would influence dermal absorption (*i.e.*, damaging the integrity of the dermal layer) further complicating the quantitative extrapolation of PODs; this aspect should be discussed.

Each of these considerations should be discussed in the route extrapolation section. EPA should also develop additional guidance for performing route-to-route extrapolations when data are lacking. At present, the draft risk evaluation for MC does not provide adequate reference to appropriate guidance for performing this approach.

[25] Geraets, L., Bessems, J.G., Zeilmaker, M.J. and Bos, P.M., 2014. Human risk assessment of dermal and inhalation exposures to chemicals assessed by route-to-route extrapolation: the necessity of kinetic data. Regulatory Toxicology and Pharmacology, 70(1), pp.54-64.

## II. Exposure Assessment

ACC acknowledges EPA's need in certain TSCA risk evaluations to use models to estimate exposure in both occupational and consumer settings when actual measured or monitored data are lacking. ACC recommends, however, that EPA's modeling efforts be improved to meet TSCA's mandates for use of best available science and weight of the scientific evidence. For example, model inputs that represent more realistic data—such as workplace volumes, weight fraction, and amount used—would improve modeled results, a necessary step. Further, while EPA indicated that it has run sensitivity models for the Consumer Exposure Model (CEM), EPA did not supply elasticity values for specific inputs. This information would help EPA focus data collection efforts on inputs that have greater impact on the model results.

### A. EPA Needs a Tiered Approach to Environmental Exposure Assessment

The agency should better explain and provide more transparency into its tiered approach to environmental exposure assessment because these approaches do not represent real world conditions. EPA applied a number of conservatisms to its estimates of environmental exposures, and specifically, surface water concentrations. While this approach may suffice for screening level assessments, they do not represent real world situations. Several points to clarify in the environmental exposure assessment section could include:

- **Volatilization**: EPA noted that due to its high Henry's law constant and vapor pressure, MC is expected to volatilize rapidly from wastewater (p. 64). However, it did not consistently or appropriately apply this aspect to its exposure estimations. For example, a number of the *Active Releasers* identified in Table Apx E-4 (pp. 572-591) are *Indirect Releasing Facilities* meaning their wastewater is piped and sent to another treatment facility typically a publicly owned treatment works (POTW). The EPA analysis does not consider dissipation in the sewers prior to wastewater treatment, also referred to as "pipe-loss."[26] In addition, EPA estimated that the half-life of MC in a model river will be 1.1 hours (p. 64); however, it did not appear to apply that half-life when considering effluent discharges to a receiving stream and the impact on downstream concentrations.
- **Dilution**: Surface water concentration estimates calculated using E-FAST for a still water body (i.e., bays, lakes, and estuaries) typically range from 1 (representing no dilution) to 200 (p. 82). However, these assumptions are unrealistically low and do not reflect the reality of the facilities evaluated. For example, the Long Beach WPCP (New York; Table 4-1, p. 289) discharges into a tidal estuary of the southern Long Island Sound. This discharge is likely to experience significantly greater dilution than assumed. EPA should conduct a more realistic, site-specific analysis for these cases where a limited number of distinct facilities appear to show unacceptable risk quotients.

[26] Matthijs E, Debaere G, Itrich NR, Masscheleyn P, Rottiers A, Stalmans M, Federle TW. The fate of detergent surfactants in sewer systems. Water Science and Technology, 1995; 31:321–328.

## B. EPA Should Clarify Its Assumptions Related to Environmental Release Scenarios

EPA states that, "[t]wenty days of release was modeled as the low-end release frequency at which possible ecological chronic risk could be determined (pp. 79-80)," and that the 20-day chronic risk criterion is derived from partial life cycle tests (p. 83).

- The 20-day release assumption should be better justified. While it may seek to replicate a worst-case situation with respect to test species, there is no basis in fact that any particular facilities discharge their effluents accordingly.
- In addition, the 20-day release scenario is coupled with 7Q10 dilution. The odds of the 20 days falling within the 7Q10 window are small and overly conservative. EPA should assume mean flow if it is going to apply an arbitrary, conservative, limited release scenario.
- Further, if this arbitrary assumption results in exceedance of the Concentration of Concern (COC), EPA should not conclude that the situation constitutes an *unreasonable risk* but that additional analysis at a higher tier would be justified.

## C. EPA Should Apply Consistent, Tiered Approaches to Dermal Modeling

Similar to the environmental discussion above, EPA must implement a tiered dermal modeling approach to ensure the dermal values considered in the assessment accurately reflect occupational conditions. In previous risk evaluations, EPA has vacillated between two different dermal models—fraction absorbed and permeability—and rationalized this process as a means to ensure protective values.[27] ACC commends EPA for adopting a uniform approach in the methylene chloride evaluation, where EPA used fraction absorbed exclusively. This model accurately accounts for methylene chloride's high vapor pressure, an important consideration when establishing absorbed doses for volatile substances. In contrast, permeability models do not typically represent realistic conditions because they assume a constant chemical supply. Furthermore, EPA must delineate a tiered-approach to exposure modeling. Modeling programs such as IHSkinPerm can produce needed detail during the exposure assessment process and ACC encourages EPA to incorporate this model into future assessments.

## D. Choices Between Low Quality and Modeled Data Must be Fully Explained

A tiered approach to exposure assessment will necessarily outline how EPA chooses which data to include in its analysis and will provide helpful guideposts when choosing between multiple problematic data. For the cold cleaning occupational condition of use, EPA utilized inhalation data from the published literature dating to 1998. These data were rated as low quality, in line with EPA's systematic review guidelines, yet EPA also ran Monte Carlo simulations for this

[27] U.S. EPA, 2019, Draft Risk Evaluation for 1-Bromopropane CASRN:106-94-5. EPA Document# EPA-740-R1-8013. Office of Chemical Safety and Pollution Prevention, U.S. Environmental Protection Agency: Washington, D.C.

condition of use, arriving at values that differed by an order of magnitude (Section 2.4.1.2.7, p. 126). Despite the published data's low-quality, EPA used these because the modeled data "[did] not capture the full range of possible exposure concentrations identified by the monitored data." As an initial matter, it is not clear from the draft risk evaluation what ranges EPA believes the monitored data captured that the modeled data did not. Further, given the available inputs in the Monte Carlo model, EPA does not explain why this model could not accommodate these ranges.

Modeling issues aside, this condition of use provides an excellent case for why EPA needs to outline a tiered approach towards exposure assessment. In this instance, there are two competing data and a cursory justification. A tiered approach could provide a scientifically-based path forward, and, if needed, suggest further steps such as a Tier 2 exposure model to achieve higher quality data. A tiered approach to exposure assessment would be more consistent with TSCA's Section 26(h) requirement for EPA to rely upon best available science in its risk evaluations.

### E. EPA Should Review Consumer Product Information for Quality

Any data that EPA incorporates as input values into consumer models must undergo a review to determine whether they reasonably depict real world conditions. EPA explains that the consumer exposure assessment uses product information obtained from safety data sheets (SDSs), particularly MC weight fraction. While SDSs are somewhat easy to obtain for some consumer products, they were developed for different purposes, and their quality, therefore, can be variable. For example as EPA notes, some ingredients are disclosed as ranges with some ranges being quite large. To ensure these input values will provide meaningful output, ACC suggests that EPA implement a quality review system for SDSs it might consider in TSCA risk evaluations, removing SDSs and associated weight fraction values that do not, on their face, represent real world conditions. Improper input values can lead to grossly overestimated exposure levels, as is the case with the coil cleaner condition of use.

### F. EPA Should Use More Realistic Scenarios for its Model Inputs for Consumer Products.

Likewise, EPA should ensure that duration and product amounts within the conditions of use represent realistic values. In modeling consumer exposures, for example, EPA estimated the duration and product amount corresponding to the 10th, 50th, and 95th percentile values based on data from the 1987 EPA publication *Household Solvent Products: A National Usage Survey*.[28] Certain durations, however, seem excessive for consumer exposures. These are more similar to occupational level exposures (Table 1-5, Draft Supplemental Information on Consumer Exposure Assessment).

- 480 minutes (8 hours) for adhesive remover
- 420 minutes (7 hours) for brush cleaner

[28] Westat, 1987; see Table 1-5, Model Input Parameters Varied by Consumer Use; Draft Risk Evaluation for Methylene Chloride Draft Supplemental Information on Consumer Exposure Assessment.

- 120 minutes (2 hours) for coil cleaner and engine cleaner.

Likewise, certain *mass of product use* assumptions for consumer exposures seem excessive:

- 2,108 g (4.65 lb) for adhesive remover
- 3,419 g (7.54 lb) for brush cleaner
- 1,268 g (2.80 lb) and 1,604 g (3.54 lb) for coil cleaner and engine cleaner, respectively

EPA should develop and/or use more current and/or relevant exposure scenarios/data to estimate the duration of use and amount of use of consumer products containing methylene chloride.

## III. Implementation of Systematic Review

As ACC has noted in comments on other risk evaluations released by EPA thus far, EPA has made progress implementing systematic review in the risk evaluations. EPA provides extensive records of the individual study quality assessments as supplemental files with the risk evaluations across chemicals, adding transparency to the reviews. However, EPA should improve transparency in the process for identifying key and supporting studies used in the evaluation, and should describe efforts undertaken to calibrate the reviews of different reviewers both within and across chemicals, as some inconsistencies in data quality evaluation remain. Further suggestions are offered below.

### A. The Study Quality Evaluation of *in vitro* Data Needs Refinement

An important factor relating to EPA's MOA and carcinogenicity assessment is the lack of a sufficient assessment of *in vitro* data quality. EPA notes in Section 3.2.3.2 (page 245), "[a] summary of genotoxicity and other mechanistic studies is also included here. EPA has not re-evaluated genotoxicity studies for quality but is relying on previous assessments, such as the IRIS assessment for detailed tables of genotoxicity study results." While it is understandable for EPA to consult the prior IRIS assessment for MC, that document did not perform a data quality assessment for genotoxicity consistent with the data quality evaluation system outlined in the Application of Systematic Review in TSCA Risk Evaluations (Systematic Review Guidance). At a minimum EPA should acknowledge that a formal data quality assessment was not performed on any cited *in vitro* studies. However, if any *in vitro* studies were used as supporting evidence in the development of a proposed MOA, they should be subject to a formal data quality assessment and the quality should be discussed in the weight of scientific evidence section.

ACC understands and supports EPA's use of a tiered approach to assessing data quality, as appropriate, where warranted. While Appendix K provides a summary of available genotoxicity data, a discussion of data quality is not included. EPA does not provide sufficient justification for this decision. Considering that EPA's conclusions regarding mutagenicity directly affect the approach needed to quantitatively assess carcinogenicity (e.g., linear versus a non-linear approach), EPA should extend study quality analysis to at least the key assays cited as supporting evidence.

More importantly, EPA should consider refining its overarching data quality evaluation framework as detailed in the Systematic Review Guidance to clarify when a full study quality evaluation *may not* be needed for each study (*e.g.,* if EPA recently evaluated study quality of some studies in a similar fashion to its TSCA guidance, another full study quality evaluation may not be necessary). The Systematic Review Guidance should specify, however, that EPA provide a description of which specific studies were evaluated or screened out, along with the rationale behind the choices to include or exclude them from data quality evaluation (*e.g*., in a table in an appendix). Along these lines, EPA could consider developing a specific tiered approach for evaluating *in vitro* data quality in which a subset of the full data quality domains deemed critical for each *in vitro* assay type are considered first, and those data quality that do not meet these criteria be considered as low quality. This may be useful in instances where data are particularly voluminous (*e.g.,* in instances of hundreds of similar bacterial mutagenicity studies), and/or conflicting results of numerous studies warrant a more efficient process for evaluating and integrating *in vitro* evidence.

### B. EPA Should Update the General Systematic Review Guidance Document to Reflect any Broadly Applicable Changes and Additional Information as It Is Developed.

The MC draft risk evaluation has applied systematic review principles to the identification, selection, and evaluation of evidence, collectively adding transparency and robustness to the risk evaluation. EPA appears to have generally followed the elements of systematic review that were addressed in its TSCA Systematic Review Guidance, while relying on existing hazard assessments of MC, where appropriate. However, when EPA published its systematic review document, it recognized that the data integration phase of the guidance was underdeveloped. The strategy for data integration lacks detail and specificity, only general, high-level principles are described, and no specific weight-of-evidence methodology is presented as a baseline for TSCA assessments. EPA indicated that it anticipated defining and demonstrating the process of integration in the first ten chemical draft risk evaluations. As EPA continues to gain more experience with data integration, and can describe the standardized procedures the Agency will use to integrate evidence that ensures consistent use of best available science, weight of the scientific evidence, and, as applicable, understanding of MOA, the Agency must update and revise this guidance document accordingly. Such a revision should include additional opportunity for review and public comment.

As described earlier, EPA indicated that it anticipated defining and demonstrating the process of integration in the first ten chemical draft risk evaluations. As EPA gains more experience with data integration, and can describe the standardized procedures the Agency will use to integrate evidence in risk evaluations (to ensure consistent use of best available science, weight of the scientific evidence, and, as applicable, understanding of MOA(s)), the Agency must update and revise this guidance document accordingly. Such a revision should include additional opportunity for review and public comment.

## IV. EPA Must Be More Transparent about Its Consultation and Coordination with the Occupational Safety and Health Administration (OSHA) and Other EPA Program Offices

### A. Coordination with OSHA

EPA and OSHA consulted on the regulation of risks from chemicals, consistent with TSCA Section 9 and a 1986 Memorandum of Understanding (MOU), long before TSCA was amended in 2016.[29] Section 9(d) requires EPA to coordinate with any other appropriate federal departments/agency (including OSHA) in order to achieve maximum enforcement of TSCA while imposing the least burdens of duplicative requirements.

Although EPA focuses on occupational exposures in the risk evaluation, in the MC draft risk evaluation, EPA has not described any consultation or coordination with any other federal agency, including OSHA. This is particularly important in the case of MC, where a detailed OSHA standard and updated PEL exist.[30] In the risk evaluation, EPA explains that it reviewed workplace inhalation monitoring data collected by OSHA and NIOSH and evaluated the data using the TSCA Systematic Review approach (p. 107). However, the context of the monitoring data is important, and whether or not the data are representative of current conditions. This is critically important as much of the data used in the draft evaluation predates the 1997 PEL. To the extent that this was discussed with OSHA, description of this discussion and consultation should be included in the risk evaluation.

Amended TSCA specifically includes workers in the definition of "potentially exposed subpopulations" and TSCA Section 6 authorizes EPA to consider workers identified as relevant subpopulations in risk evaluations and impose "restrictions" on manufacturing/processing on the basis of an unreasonable risk determination concerning the health of workers. However, these changes do not mean that EPA stands in the shoes of OSHA on chemical risk issues in the workplace. TSCA Section 9 still authorizes OSHA to decide whether it agrees with EPA's risk determination concerning worker health and its recommendations for risk management. With the continued need for EPA and OSHA to consult on chemical matters in the workplace, EPA must be more transparent in its risk evaluations about its consultations with OSHA.

### B. TSCA Section 9 Coordination with Other EPA Program Offices in the Longer Term

EPA OPPT's decision to "scope in" the ambient water pathway and to conduct an aquatic life risk evaluation in the MC draft TSCA risk evaluation raises serious questions about the overlapping jurisdiction of TSCA and other environmental laws, the TSCA Section 9 coordination requirements, and EPA's ability to efficiently conduct risk evaluations in the longer term.

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[29] Available at https://www.osha.gov/laws-regs/mou/1986-02-06.
[30] OSHA Standard for Methylene Chloride at 29 CFR 1910.1052.

ACC has consistently recommended (in the comments on each of the draft risk evaluations to date) that to satisfy Section 9's coordination requirements, as well as TSCA's call for increased transparency in decision-making, EPA should provide more information in it scoping documents and draft risk evaluations about how it determines whether existing regulations under other statutes are adequate to address potential risks associated with a TSCA chemical under certain conditions of use. ACC continues to support this recommendation, but it is not enough.

EPA OPPT's scoping decision and its review of the ambient water pathway in the MC draft risk evaluation raise questions about EPA OPPT's decision-making process with respect to consideration of the "disposal" condition of use. It also raises questions about EPA OPPT's level of expertise in regulating "disposal" to air, water and soil, and about achieving efficiencies in EPA OPPT's risk evaluations.

To resolve these issues, ACC strongly recommends that EPA OPPT convene a broader discussion with other EPA program offices about how – in the longer term – it should seek to: a) better understand the regulatory requirements and processes of the various environmental statutes under EPA's purview; b) reach agreement on the value (or not) of EPA's potential use of TSCA risk evaluations to address air, water, and other waste pathways under the TSCA disposal condition of use; and c) to establish better approaches for coordinating what each program office (including EPA OPPT) can provide the others to improve environmental protection under their respective statutory authorities more efficiently and without duplication.

1. **The methylene chloride scoping and draft risk evaluation example ignored long-standing regulation of the chemical under the Clean Water Act.**

Methylene chloride's problem formulation document's discussion at 2.5.3.3 (page 54) on "Pathways that EPA Does Not Expect to Include in the Risk Evaluation" opened with the statement that, ***"EPA does not expect to include in the risk evaluation pathways under programs of other environmental statutes, administered by EPA, which adequately assess and effectively manage exposure and for which long-standing regulatory and analytical processes already exist."*** EPA then proceeds to explain why it did not expect to evaluate air emission pathways (because MC is regulated as a Clean Air Act hazardous air pollutant), or the drinking water pathway (because MC is currently addressed in the SDWA regulatory process), or landfill/incineration/injection disposal pathways (because MC is a listed hazardous waste under RCRA).

With respect to ambient water pathways, however, in section 2.5.3.3 of the problem formulation document, EPA noted that the EPA Office of Water had developed a water quality criteria for MC to protect human health, but that the Office of Water had not developed a criteria for protection of aquatic life. So EPA concluded, ***"As a result, this pathway will undergo aquatic life risk evaluation under TSCA. EPA may publish CWA section 304(a) aquatic life criteria for methylene chloride in the future if it is identified as a priority under the CWA."***

This conclusion was not supported by any further explanation. Without more discussion, it appears to have ignored the Office of Water's extensive and long-standing regulation of MC under the Clean Water Act (CWA). MC has been categorized by the Office of Water as a CWA toxic pollutant/priority pollutant since 1977, and has been regulated under the Clean Water Act's technology based effluent limitation guidelines since the 1980s. Mandatory effluent limitation guidelines have been set for MC at "best available technology (BAT)" levels for both CWA direct discharges of MC from regulated industries and pretreatment limits for CWA indirect discharges of MC to wastewater treatment facilities. These limits are incorporated into CWA National Pollutant Discharge Elimination System (NPDES) permits for industries that discharge methylene chloride. Moreover, these federally mandated technology based standards for methylene chloride are within the same order of magnitude as the water quality based human health criteria (e.g. 89 ug/L technology based standard vs 20 ug/L HH criteria.)

2. **The basis for EPA OPPT's decision to address the ambient water pathway doesn't account for the Clean Water Act's water quality criteria and standard setting processes.**

Moreover, EPA OPPT's decision to address potential risks to aquatic life in the ambient water pathway – due to the absence of a CWA Section 304(a) aquatic life criteria -- appears to overlook the fact that EPA's numeric water quality criteria for protection of aquatic life/human health are **guidance** for the states that implement the CWA's NPDES program. They are not mandatory regulatory requirements unless/until they are incorporated into NPDES permits. EPA establishes water quality criteria for the States to use when they need tighter standards than the technology standards can provide to protect specific designated uses of State waterbodies. Narrative water quality criteria, however, (e.g. pollutants must not be present in harmful concentrations) are also commonplace in NPDES permits to enable the States to act to prevent water quality issues that are not addressed by specific chemical pollutant restrictions in permits.

In addition, in the draft risk evaluation, EPA OPPT effectively second-guessed the Office of Water's decision about the **need** for an aquatic life criteria on MC. There is no requirement under CWA Section 304(a) for EPA to establish WQ criteria for all pollutants that may be discharged into waters of the US. The CWA, just as in TSCA, must prioritize its actions to meet the statute's goals. As EPA's own *Guidelines for Deriving Numerical National Water Quality Criteria for the Protection of Aquatic Organisms and Their Uses* (1985) states, "Derivation of national water quality criteria for the protection of aquatic organisms and their uses is a complex process that uses information from many areas of aquatic toxicology."[31] MC is a highly volatile compound. Volatility is one of those properties that "might affect the fate of a material in the aquatic environment and might be important when determining whether a criterion is needed for a material."[32] The guidelines further emphasize the critical importance of EPA having appropriate data before criteria can be developed, stating that, "It is not enough that a national criterion be the best estimate that can be obtained using available data; it is equally important that a criterion be derived only if adequate appropriate data are available to provide reasonable confidence that it is a good estimate. Therefore, these National Guidelines specify certain data that should be available if a numerical criterion is to be derived."[33] In other words, not all pollutants are candidates for CWA Section 304(a) numeric water quality criteria for a variety of

[31] U. S. Environmental Protection Agency, 1985, Guidelines for Deriving Numerical National Water Quality Criteria for the Protection of Aquatic Organisms and Their Uses, by Charles E. Stephen, Donald I. Mount, David J. Hansen, John R. Gentile, Gary A. Chapman, and William A. Brungs, Office of Research and Development, Environmental Research Laboratories, Duluth, MN, Narragansett, RI, Corvallis, OR, p. iv.

[32] Ibid, page 8.

[33] Ibid, page 3.

sound reasons (the pollutant's physical/chemical properties; its fate in the ambient water; the existence of data to support the derivation of a criteria.)

### 3. Recommendations Going Forward

With specific respect to OPPT's consideration of the ambient water pathway in future TSCA risk evaluations, the mere absence of an EPA-developed water quality criteria on aquatic life (or human health) should not in and of itself trigger inclusion of consideration of ambient water pathways in a TSCA risk evaluation. The CWA achieves its statutory objectives by requiring CWA discharges to comply with the more restrictive of applicable water quality based and technology based requirements. The CWA focuses on "priority" pollutants, not all pollutants or all chemicals on the TSCA Inventory. The biological treatment of BAT limitations, for instance, does not treat just the named pollutants in a discharge permit, but all of the pollutants in an industry's waste stream. EPA OPPT should not discount the existence of mandatory, technology based effluent limitations and narrative water quality criteria from consideration in deciding whether to scope water pathways in or out of a TSCA risk evaluation. In addition to the technology based limitations, Clean Water Act water quality criteria provide guidance to states to establish water quality standards to protect water quality for particular waterbody uses in their states. In other words, water quality guidance criteria, once incorporated into a State's water quality standard, are State, waterbody and permit specific. They are not applied in all CWA NPDES permits.

EPA OPPT's policy decision to scope in the potential risks of MC from exposure to aquatic life resulted in a complex examination of the potential for methylene chloride to present an unreasonable risk to aquatic life under the recycling and disposal conditions of use. EPA's review of studies and its development of benchmarks acknowledged uncertainties in data, but ultimately concludes there is "no unreasonable risk" to aquatic life from the recycling/disposal condition of use of MC.

EPA OPPT should summarize in its draft risk evaluations any discussion with the Office of Water that took place regarding: the need for a TSCA evaluation of the ambient water pathway in a TSCA condition of use; whether the Office of Water supported EPA OPPT's decision; whether EPA OPPT used what the Office of Water would consider the "best available science" to characterize this risk; whether the efficiencies of undertaking this evaluation versus asking the Office of Water to consider developing an aquatic life water quality criteria for MC were considered; etc.

TSCA was never intended to replace regulation by other EPA environmental programs, each of which has different requirements and standards and approaches for regulatory decision-making. EPA OPPT's decision to scope in and review the ambient water pathway for MC raises questions about the degree of coordination EPA OPPT had with the Office of Water as required by TSCA Section 9. A longer term re-thinking of EPA OPPT's approach to coordinating with other EPA program offices, and the establishment of a better process, is in order -- both to ensure protection of our air, water and soil and to enable EPA OPPT to meet its statutory obligations to conduct TSCA risk evaluations of high priority chemicals efficiently and in accordance with the best available science.

## V. TSCA Risk Evaluations Should Employ a Consistent Format and Make Clearer How EPA's Risk Characterization Supports its Risk Determinations.

While every chemical's risk evaluation will rely upon different scientific information, assumptions, and uncertainties, the basic format by which EPA presents that information should be consistent, as much as possible. The unreasonable risk determination (for MC at Table 5-1), in particular, is important for communication of information regarding conditions of use, risk estimates, benchmarks, risk drivers, and risk determinations. This is a lot of information to contain in one large table, in particular for MC where there are many conditions of use. EPA has made some improvements and streamlined this table somewhat as compared to previous risk evaluations, such as the inclusion of citations to the relevant sections in the risk characterization to point the reader to the supporting evidence. There are still improvements that can be made, however.

For better risk communication about its risk determinations, EPA should boldface both the "presents" and the "does not present" statements in Table 5-1. For better risk communication about the basis of its risk determinations, EPA's "presents" and "does not present" statements should cite to the Section 26 statutory and regulatory requirements that the determinations are based upon best available science, weight of the scientific evidence and data quality. EPA should consider including a modified table that represents the relevant endpoints and drivers, potentially color-coded with regard to those that exceed benchmarks.

There are several risk assessment models that EPA might use to communicate its TSCA risk characterizations. One comes immediately to mind: HESI's Risk21 Project and Web Tool. The RISK21 web tool application allows users to create a plot of exposure and toxicity data for chemicals, overlaying a risk matrix represented as a heat map. [34,35] This provides a clear and effective visual representation of the range of potential risks, including representation that is particularly effective for risk communication purposes. The below graphic, taken from Pastoor et al. (2014), provides an overview of the RISK21 Process, including:

1) Problem formulation: Define problem. This initial step is reevaluated throughout the iterative process;

2) Exposure estimate: Obtain tiered estimate of exposure BEFORE assessing toxicity. Use existing knowledge. Express as range;

3) Toxicity estimate: Obtain tiered estimate of toxicity. Use existing knowledge. Develop data only as needed. Express as range;

4) Matrix: Intersect exposure and toxicity estimates on the matrix.[36]

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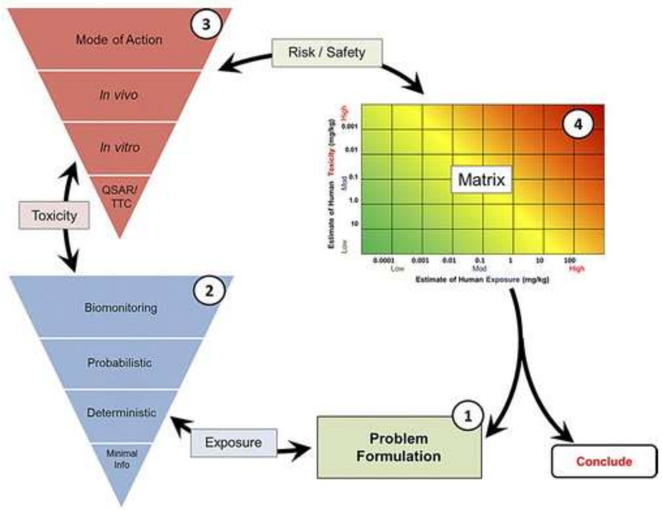
[34] Michelle R. Embry, Ammie N. Bachman, David R. Bell, Alan R. Boobis, Samuel M. Cohen, Michael Dellarco, Ian C. Dewhurst, Nancy G. Doerrer, Ronald N. Hines, Angelo Moretto, Timothy P. Pastoor, Richard D. Phillips, J. Craig Rowlands, Jennifer Y. Tanir, Douglas C. Wolf & John E. Doe (2014) Risk assessment in the 21st century: Roadmap and matrix, Critical Reviews in Toxicology, 44:sup3, 6-16, DOI: 10.3109/10408444.2014.931924.

[35] Timothy P. Pastoor, Ammie N. Bachman, David R. Bell, Samuel M. Cohen, Michael Dellarco, Ian C. Dewhurst, John E. Doe, Nancy G. Doerrer, Michelle R. Embry, Ronald N. Hines, Angelo Moretto, Richard D. Phillips, J. Craig Rowlands, Jennifer Y. Tanir, Douglas C. Wolf & Alan R. Boobis (2014) A 21st century roadmap for human health risk assessment, Critical Reviews in Toxicology, 44:sup3, 1-5, DOI: 10.3109/10408444.2014.931923

[36] *Id.,* at p. 4, Figure 1.




This methodology aligns with EPA's approach as detailed in the Risk Evaluation Rule. EPA should consider this approach, or a similar approach that provides an effective visual representation of the potential range of risks, to aid in communication of the risk characterization for the conditions of use.