Comments on HBCD

30. EPA has excluded or failed to sufficiently analyze numerous conditions of use and exposure pathways for HBCD.

A. EPA has inappropriately excluded legacy uses, associated disposal, and legacy disposal of HBCD from the problem formulation.

EPA intends to exclude multiple conditions of use of HBCD based on the condition of use allegedly being "legacy." EPA should consider all of these conditions of use for reasons articulated before and incorporated by reference here. EDF Comments on Ten Scopes under the Toxic Substances Control Act, pp. 4-11 (Sept. 2017), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0743-0069; Appendix A.

Use in High Impact Polystyrene: First, EPA has excluded the use of HBCD in High Impact Polystyrene (HIPS) as a flame retardant for electrical and electronic appliances because its use "appears to have ceased." U.S. EPA, Problem Formulation for Cyclic Aliphatic Bromides Cluster (HBCD) at p. 21 (May 2018), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0735-0071. Notably, EPA's source for this caveated assumption is a single personal communication with one company, which EPA has not corroborated and the substance of which EPA has not made available. This is unacceptable.[136] To base a wholesale exclusion of a condition of use on such a flimsy extent of documentation that the public cannot access is simply outrageous. How is the public supposed to assess the accuracy and reliability of this comment? Moreover, that one person at one company reports that the company has ceased a particular use provides no assurance that other companies are not continuing the use. In addition, such personal communications do not reflect the best available science because EPA has failed to rely on all reasonably available information. EPA has broad authority under TSCA § 8 to require reporting industry wide under binding rules with various measures to increase reliability, and thus such broad reporting is reasonably available to EPA; EPA cannot rationally rely on unverified and potentially unrepresentative personal communications instead.

In addition to the reasons identified previously for why legacy uses must be included, *see* Section 4.A, EPA should include the use of HIPS as a condition of use because the agency has insufficient evidence that the use has stopped.

EPA states that it "believes the manufacturing, processing, or distribution in commerce for use of HBCD as a flame retardant in HIPS is not intended, known, or reasonably foreseen and is not a condition of use of HBCD." (p. 21) Even assuming EPA is correct that such use is no longer occurring and hence is not "known," that is no basis to conclude it is also not "reasonably foreseen." Congress distinguished between "known" and "reasonably foreseen" in its definition of conditions of use, and EPA cannot

[136] This personal communication is not in the docket, nor is it listed in the bibliography for this problem formulation.

equate the two. Barring a regulatory prohibition on such use, EPA has no basis for concluding the use is not reasonably foreseen and hence cannot exclude it from the risk evaluation.

Following from this exclusion, EPA is also excluding the disposal of HBCD-containing HIPS and HIPS-containing electronic products as "associated disposal." (p. 21) This will result in EPA disregarding any exposures to HBCD from the management of electronic waste.[137] EPA cannot rationally ignore these ongoing exposures.

Manufacture of EPS Resin and XPS Masterbatch: EPA is excluding the manufacture of expanded polystyrene (EPS) resin and extruded polystyrene (XPS) because these uses have been phased out, allegedly, by their "major" manufacturers. (p. 21) This exclusion raises a number of concerns. First, although one comment on EPS from an industry representative is publicly available, the comment EPA cites regarding XPS is not. EPA's source for this assertion about XPS is a single personal communication with a trade association representative, which EPA has not corroborated and the substance of which EPA has not made available. This is unacceptable.[138] EPA must make this publicly available.

Second, even assuming EPA is correct that "major" manufacturers have phased out manufacture of EPS and XPS, EPA appears to have made no attempt to determine whether there are other manufacturers of EPS and XPS. EPA cannot assume that communications from representatives of the major manufacturers accurately reflects the status of *all* users of HBCD in EPS and XPS.

Lastly, even assuming that this use of HBCD has been "phased out" and that the industry has "fully transitioned" from it, that is no basis to conclude the use is also not "reasonably foreseen." Congress distinguished between "known" and "reasonably foreseen" in its definition of conditions of use, and EPA cannot equate the two. Barring a regulatory prohibition on such use, EPA has no basis for concluding the use is not reasonably foreseen and hence cannot exclude it from the risk evaluation.[139]

Use in Textiles: EPA is also excluding the use of HBCD in consumer textiles, including interior fabrics in motor vehicles and children's clothing and blankets, on the basis of it being a legacy use. (p. 22) The basis for this exclusion is also a personal communication from an industry source that is not publicly

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[137] In addition to exposures from the release of HBCD from electronic waste, it appears that the disposal of HIPS (and HBCD) may occur in other ways that would likely result in exposures. *See* Using D-Limonene to Dissolve 3D Printing Support Structures (Apr. 2014), https://www.fargo3dprinting.com/using-d-limonene-dissolve-3d-printing-support-structures/ (suggesting that the product can be disposed of in the sink); *see also* HIPS Filaments, https://www.3dprima.com/filaments/hips/ (last visited Aug. 8, 2018) (noting, on a product page, that "[f]rom time to time manufacturers add flame retardants like DecaBDE or HBCD to the matrix").

[138] This personal communication is not in the docket, nor is it listed in the bibliography for this problem formulation. The link in the document goes to a webpage that provides no transcript of the "personal communication."

[139] EPA cites an international ban as a reason for the phase-out of this use. (p. 21) But as EPA itself noted, (p. 31), the U.S. is not a party to the Stockholm Convention on Persistent Organic Pollutants, which banned the use, import, and export of HBCD. Moreover, under the Convention, three parties are registered to produce HBCD and six are registered to use HBCD for EPS and XPS in foam.

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available. This too is unacceptable.[140] Moreover, information EPA cites directly contradicts this rationale: Between June 2012 and March 2017, the presence of HBCD in textile products was reported by industry 44 times to Washington State. (p. 22) While EPA speculates that such items would now be caught by a SNUR it has finalized, this is not a basis for dismissing such evidence of continued use.

EPA states that "[c]urrent use in consumer textiles has not been confirmed and EPA does not believe it is known, intended, or reasonably foreseen. Therefore, use in consumer textiles is not a condition of use under which EPA will evaluate HBCD." (p. 21) As discussed above, even if this use is no longer occurring and hence is not "known," that is no basis to conclude it is also not "reasonably foreseen" that the use may begin again. The definition of conditions of use expressly distinguishes between "known" and "reasonably foreseen," therefore EPA cannot equate the two. Barring a regulatory prohibition on such use, EPA has no basis for concluding the use is not reasonably foreseen and hence cannot exclude it from the risk evaluation.

In a further effort to avoid including these uses, EPA "concluded" that these products did not contain "intentionally-added" HBCD. (p. 22) However, EPA chose not to explain to the public just how it reached this conclusion. It needs to do so.

Even so, while EPA asserted in the final Risk Evaluation rule that it may ignore impurities that are "unintentionally" present in another chemical substance, nowhere does EPA explain in the rule, or in this problem formulation, that it has discretion to exclude a use because it is not "intentionally added" to consumer products. 82 Fed. Reg. 33726, 33729-30 (Jul. 20, 2017). Even assuming EPA's assertion about such products is true, that is no basis to conclude it is not "known" or "reasonably foreseen." Congress specified that conditions of use extended beyond "intentioned" circumstances to include "known" and "reasonably foreseen" circumstances, and EPA has no basis for concluding that the use of HBCD in a product is not known or reasonably foreseen merely because it is not "intentionally added."

EPA also excludes commercial textiles because the use is not "ongoing." (p. 22) The basis for this assertion is several personal communications that EPA has not corroborated, one from a source identified only by partial name (Friddle, J.) without any affiliation. None of these personal communications is publicly available. As noted before, this is unacceptable,[141] and it provides no basis for the public to assess the accuracy or reliability of these communications.

EPA notes that, as of quite recently, HBCD has been used in textiles in the military, institutional and aviation applications, and hospitals and prisons. EPA states that:

> Current use in commercial textiles could not been [sic] confirmed, but EPA concludes that based on the information above, HBCD use in these textiles is not intended, known,

[140] This personal communication is not in the docket, nor is it listed in the bibliography for this problem formulation.

[141] This personal communication is not in the docket, nor is it listed in the bibliography for this problem formulation.

> or reasonably foreseen. Therefore, use in commercial textiles is not a condition of use under which EPA will evaluate HBCD. (p. 22)

Even assuming EPA is correct that such use is no longer occurring and hence is not "known," that is no basis to have concluded it is also not "reasonably foreseen." Congress distinguished between "known" and "reasonably foreseen" in its definition of conditions of use, and EPA cannot equate the two. Barring a regulatory prohibition on such use, EPA has no basis for concluding the use is not reasonably foreseen and hence cannot exclude it from the risk evaluation.

This exclusion is also concerning because of the potential for exposures associated with the *disposal* of these products. EPA does not even acknowledge that the disposal of commercial textiles will occur. While EPA may argue that the disposal of commercial textiles falls under its legacy-related category of "associated disposal," as described earlier in these comments (Section 4.A), EPA has no basis in the law for excluding such conditions of use. Both the use and disposal of HBCD-containing commercial textiles should be included in the risk evaluation.

Use in Adhesives: EPA has excluded use of HBCD in adhesives because, in January 2018, EPA had a personal communication with one company that manufactured an adhesive with HBCD, which apparently told EPA that, despite the use of the chemical being publicly noted on a 2017 MSDS,[142] "the company *will no longer* use HBCD in their product line." (p. 22, emphasis added) This personal communication from the industry source, which EPA has not corroborated, is not publicly available. As noted before, this is unacceptable.[143] According to EPA, the company "does not have a current supply of HBCD" and "will no longer use HBCD." (p. 22) No timeline was indicated, however, as to when the company will cease selling such products. Considering how recent this communication is, and that it involves only one company, EPA cannot on this basis determine that all such use of the chemical has or soon will cease.

EPA states: "EPA could find no evidence of ongoing manufacture, processing or distribution of adhesives using HBCD. Therefore, adhesives are not included as a condition of use for which EPA will evaluate HBCD." (pp. 22-3) Even assuming EPA is correct that such use is no longer occurring and hence is not "known," that is no basis to concluded it is also not "reasonably foreseen." Congress distinguished between "known" and "reasonably foreseen" in its definition of conditions of use, and EPA cannot equate the two. Barring a regulatory prohibition on such use, EPA has no basis for concluding the use is not reasonably foreseen and hence cannot exclude it from the risk evaluation.

Use in Automotive Sector: EPA has excluded use of HBCD in the manufacture of new automobiles from the risk evaluation, based on EPA's view that the use is not ongoing. Only its use in replacement parts is to be included.

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[142] For reasons that are not clear, the link EPA provides to this MSDS does not link to the MSDS. And the link from the EPA HERO database does not link to the MSDS either.

[143] This personal communication is not in the docket, nor is it listed in the bibliography for this problem formulation.

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EPA bases this exclusion largely on three comments received from industry associations (p. 23) that are inconsistent and conflicting and that EPA then misinterprets. The first two commenters assert that HBCD is not used in the "manufacture of new vehicles" or "during the manufacturing process of any automotive components." These assertions are explicitly or implicitly limited to the members of those industry associations, however. The third commenter, the Alliance of Automotive Manufacturers, indicates that "this chemical is not used *during the auto manufacturing process*."[144] But the commenter goes on to state:

> However, the chemical may still be *used by some automakers* as a flame retardant in coatings of *certain components* (e.g., dashboards and headliners) and in solder paste in interior components (e.g., circuits). This chemical may also be present in adhesives and foams. (p. 23, emphases added)

This third comment, which contradicts the others, does not limit HBCD's scope to replacement parts at all, and should clearly be read as applying to *components* used in new automobiles, though not to use in *the auto manufacturing process* itself. Thus, the evidence before the agency indicates that HBCD may still be used in components of new automobiles.

Later in the document, EPA states:

> Major automobile manufacturers have phased out use of HBCD in U.S. production but continue to use it in a *few replacement parts*, according to information provided to EPA by the Alliance of Automotive Manufacturers since publication of the HBCD Scope Document. Manufacturers identified three replacement parts containing HBCD, these are absorbers (front roof rail energy) and two types of insulator panels (Alliance of Automobile Manufacturers, 2018). (p. 27, emphasis added)

The reference provided by EPA, (Alliance of Automobile Manufacturers, 2018), is yet another personal communication that EPA has not corroborated and that is not publicly available. Again, this is unacceptable.[145] The source is the same as the third commenter noted above, however, and EPA's summation of the personal communication is at odds with the earlier comment by the commenter, which is publicly available. There is no way for the public to ascertain whether the apparent contradiction is due to an inaccuracy in EPA's summary or a change in the industry association's assertion.

In any case, given this conflicting information and lack of public access to information on which EPA is relying, EPA cannot support its contention, more sweeping than its cited sources support, that "use of HBCD in the manufacture of new automobiles is not occurring (U.S. EPA, 2017c, 2012d, 2006b).

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[144] This comment's reference to use "during the auto manufacturing process" is decidedly narrower than the scope of EPA's conclusion drawn from it that applies to use "in the manufacture of new automobiles."

[145] This personal communication is not in the docket, nor is it listed in the bibliography for this problem formulation.

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Therefore, the use of HBCD in manufacture of new automobiles is not intended, known, or reasonably foreseen and therefore is not a condition of use under which EPA will evaluate HBCD." (p. 23)

Furthermore, as stated above, even assuming EPA is correct that such use is no longer occurring that is no basis to concluded it is also not "reasonably foreseen." Without a ban on this use, EPA has no basis for concluding the use is not reasonably foreseen and hence cannot exclude it from the risk evaluation.

Disposal: Although not directly addressed by EPA in the problem formulation, EPA entirely fails to mention, and hence presumably intends to exclude, so-called "legacy disposal" of HBCD-containing materials. This exclusion is especially concerning because, as EPA notes, HBCD is persistent and bioaccumulative. (p. 51) According to the problem formulation, "HBCD has been detected in a wide variety of environmental media[,] *** [and] [h]as been detected in remote areas from long range transport." (p. 35) Although EPA states that it will consider emissions to air, releases to surface waters and sediment, and application to soil of biosolids from wastewater treatment, including from disposal of HBCD or HBCD-containing materials from ongoing uses (p. 50), it is entirely unclear how EPA intends to distinguish between releases and exposures from past so-called "legacy disposals," ongoing so-called "associated disposals" of HBCD from discontinued uses, and ongoing disposal of HBCD from ongoing uses, when the chemical is so prevalent in all environmental media.[146] As EPA stated "[t]here have been changes to use patterns of HBCD over the last few years," making this analysis even more challenging. (p. 62) This issue highlights the arbitrariness and lack of scientific basis for EPA's artificial distinctions between these categories of disposal. EPA must not underestimate exposure to HBCD based on arbitrary distinctions between the sources of the contamination.

Domestic Manufacturing: Additionally, while EPA does not deem domestic manufacturing of HBCD to be a legacy condition of use, EPA has excluded it because EPA asserts the activity has recently ceased. (p. 20) EPA states in the problem formulation that it reached out to two U.S. manufacturers who indicated that they had completely replaced HBCD in their product lines and that use of stockpiles and exportation was completed in 2017. EPA received communications from the two companies that indicated they "d[id] not intend" to manufacture, import, or export HBCD in the future. (p. 20) These four personal communications linked to in the problem formulation, which EPA has not corroborated, are not publicly available. Once again, this is unacceptable.[147]

These communications, even if accurate, do not demonstrate that all domestic manufacture of HBCD has permanently ceased. While the two companies EPA communicated with were the only companies that reported domestic manufacture under the 2016 CDR, four other companies reported import of

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[146] Elsewhere, in the context of occupational exposures, EPA itself raises the need to apportion exposures to different sources: "[i]n an effort to associate exposure estimates with sources of exposure and/or conditions of use, EPA will consider source apportionment across exposure scenarios during risk evaluation. EPA anticipates that there will be a wide range in the relative exposure potential of the exposure scenarios identified in Appendix C." (p. 66)

[147] These personal communications are not in the docket, nor are they listed in the bibliography for this problem formulation.

HBCD, according to EPA's Use and Market Profile for Hexabromocyclododecane,[148] and some of these companies have domestic chemical production facilities. CDR reporting is subject to various reporting thresholds and exemptions, which means these or additional companies may domestically produce HBCD but did not report under the CDR because they fell below the volume thresholds or qualified for an exemption. Indeed, Table A-1 of EPA's Use and Market Profile for Hexabromocyclododecane lists three U.S. companies as domestic producers of HBCD that are not among the six companies that reported under the CDR. EPA appears to have had no communications with these companies, and apparently no basis for concluding that they have ceased domestic production.

As EPA stated in the problem formulation, the U.S. is not a party to the Stockholm Convention on Persistent Organic Pollutants, which banned the use, import, and export of HBCD. (p. 31) Under the Convention, three parties are registered to produce HBCD and six are registered to use HBCD for EPS and XPS in foam. (p. 31) While it is certainly progress that some U.S. manufacturers appear to have voluntarily chosen to discontinue manufacture, import, and export of HBCD, absent a regulatory ban in the U.S., there is not any assurance that such activities will not resume. Hence there is no basis to conclude the condition of use is not "reasonably foreseen." Congress distinguished between "known" and "reasonably foreseen" in its definition of conditions of use, and EPA cannot equate the two. Hence EPA cannot exclude it from the risk evaluation.

Need for a Significant New Use Rule: Because EPA has chosen to exclude all of these conditions of use for HBCD, EPA should at least promulgate a Significant New Use Rule (SNUR) as it has proposed to do for certain legacy uses of asbestos. *See* 83 Fed. Reg. 26922 (June 11, 2018), https://www.federalregister.gov/documents/2018/06/11/2018-12513/asbestos-significant-new-use-rule. Notably, for at least one of these uses, there is already a SNUR: EPA finalized a SNUR in 2015 for HBCD in consumer textiles. (p. 21) Especially where EPA has indicated that some of these uses have either yet to end or ended as recently as January 2018, at a minimum, EPA must put a SNUR in place promptly after their cessation, to ensure these uses do not begin again in the future without at least prior notification to EPA.

B. EPA's bases for excluding other conditions of use are unlawful.

Recycling of HIPS: While EPA is excluding the use of HIPS in electronic products because EPA deems it a so-called legacy use, it appears that EPA is excluding the recycling of HIPS-containing electronic products on a different basis. (p. 21) Despite recognizing that electronic products can be recycled and that HIPS-containing materials constitute more than half of the plastic materials recovered from household electronics, EPA is excluding this use because "no information was identified that confirms use of HBCD in recycled HIPS for the *purposes of flame retardancy*." (p. 21) EPA has never articulated an exclusion of conditions of use on the basis that the function served by an ongoing use is different than the function associated with a use that EPA now considers "legacy."[149] First, whether a chemical present in a

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[148] *See* Use and Market Profile for Hexabromocyclododecane (HBCD) at 7 (June 2017), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0735-0049.

[149] Moreover, EPA states that "[n]o information was identified that further described the processes used in recovering the plastics from electronics and how those plastics are reprocessed into other

material is serving a particular function or not has no bearing on its exposure potential, and thus EPA should be analyzing HBCD in these recycled products to obtain a scientifically accurate assessment of exposure. Second, EPA must address the risks of a chemical under its conditions of use, defined under TSCA § 3(4) to extend to known or reasonably foreseen, as well as intended, circumstances. Thus, EPA cannot exclude exposures that are known or reasonably foreseen even if they are not intended. EPA must gather the necessary information on these uses, and address any exposures from these ongoing uses.

Recycling of EPS/XPS: Additionally, despite the fact that "the primary on-going consumer use of HBCD is within EPS and XPS insulation" *and* that EPA plans to analyze certain conditions of use associated with the recycling of articles containing HBCD back into EPS and XPS insulation, EPA will only do so when the HBCD in those articles imparts intended flame retardancy to the final product. (p. 37) This exclusion has no basis in the law, or in EPA's regulations. EPA must assess HBCD in all recycled products.

Other uses: EPA also decided that a number of uses are not conditions of use, specifically, "coatings, solder, children's products including toys and car seats; furniture (such as bean bags chairs)." (p. 24) In regards to the children's products, EPA has evidence that HBCD is present in some children's products. (pp. 23-24) It appears that because the Washington state legislature determined that HBCD was not added to the products for purposes of flame retardancy, (p. 24), EPA does not consider its presence in children's products to be a "condition of use." This "reasoning" entirely fails to consider that HBCD *is present in children's products* and is therefore a known condition of use.

Also, for certain additional uses that were identified, EPA states it is "uncertain whether similar U.S. products contain HBCD. In some of the articles, HBCD is present but may not have been intentionally used." (p. 26 fn.e) But Congress directed EPA to assess chemical risks associated with reasonably foreseen and known, as well as intended, circumstances under which a chemical substance may be manufactured, processed, distributed in commerce, used, or disposed of. 15 U.S.C. § 2602(4). Evidence of HBCD's presence in products in the U.S. means that it is known or reasonably foreseen that consumers in the U.S. may use such products or otherwise be exposed to HBCD present in the products; therefore, such uses are conditions of use of HBCD. It is not clear from EPA's citation what these uses are; however, an article from 2014 indicates that there may be additional products where HBCD is present that EPA has not addressed in the problem formulation.[150]

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products." (p. 89). In light of this data gap, how can EPA reliably conclude what the purpose is of the recycled products?

[150] Manviri Rani, et al., *Hexabromocyclododecane in polystyrene based consumer products: An evidence of unregulated use*, 110 Chemosphere at 111-19 (Sept. 2014), https://www.sciencedirect.com/science/article/pii/S0045653514002252 (identifying marine buoys and food containers, among other items, has having concentrations of HBCD). This document is mentioned in EPA's bibliography on HBCD, so it is unclear why EPA would not have addressed these potential uses.

C. EPA must further analyze drinking water as a potential exposure pathway to HBCD.

EPA stated that there is potential for oral exposure to HBCD by "ingestion of dust and soil; *drinking water* and breast milk; and edible aquatic and terrestrial biota (e.g., from fishing, hunting, gathering and farming)." (p. 38, emphasis added) However, EPA states it does not expect to further analyze exposures from drinking water sources. (pp. 38, 51) This pathway is excluded despite the fact that "drinking water monitoring data is generally unavailable." (p. 38) EPA even acknowledges that "exposures from drinking water containing HBCD are possible," but nevertheless excludes these exposures because they "are likely to be relatively lower than other oral exposure pathways." (p. 51) But TSCA includes nothing that allows EPA to limit itself only to assessing the "relatively larger" sources of exposure to HBCD or other chemicals. Ultimately, EPA relies solely on the physical-chemical and fate properties of HBCD to predict that the concentrations of HBCD in drinking water will be low. But EPA has not established that these concentrations and exposures will not be significant, particularly in conjunction with other exposure pathways. EPA should obtain additional information on this exposure pathway and analyze this pathway.

D. EPA should not exclude disposal of HBCD on the basis of other statutory authorities.

EPA will explicitly exclude all disposal pathways except disposal of construction and demolition wastes to RCRA subtitle D municipal solid waste landfills. (p. 52) EPA has failed to provide any analysis to demonstrate the extent to which existing regulations actually eliminate associated exposures. As discussed earlier in these comments at length, such statute-based exclusions have no basis in the law and are scientifically unsound (see Section 5.F).

E. EPA has improperly decided to do no further analysis on a number of human exposure pathways to HBCD.

Occupational Exposures: EPA states it generally plans to consider exposures to workers and occupational non-users (ONU). However, in the case of automobile replacement parts, EPA plans to do no further analysis on dermal and inhalation exposures to workers because "emissions of HBCD from automobile replacement parts are not expected to be significant and the EPS or XPS that comprises these replacement parts is expected to be covered with other material thereby limiting emissions." (p. 97) These statements raise numerous concerns. EPA indicated this decision by listing it in a table without any additional explanation or citation to support its "expectations." As a result, it is entirely unclear what EPA considers to be an "insignificant" level of emissions from HBCD and how it made that determination. Presumably workers are involved in applying any covering present in such parts in the first place and hence may have been exposed prior to its application. Considering that EPA is generally analyzing inhalation for all other exposure scenarios, this cursory explanation to do no further analysis of this exposure to workers is arbitrary and lacks justification.

EPA will also fail to analyze nearly all ONU *dermal* exposures to HBCD for the majority of the release exposure scenarios for the industrial/commercial uses of HBCD. Specifically, EPA is doing no further analysis on all but one potential dermal exposure because "[d]ermal exposure is expected to be primarily to workers directly involved in working with the chemical." (pp. 95-98) TSCA provides no basis

for limiting EPA's risk consideration only to direct exposures, nor to focus only on persons "primarily" exposed to the chemical.

EPA also expects to do no further analysis on worker exposure to HBCD during the distribution of bulk materials or formulated products through any exposure pathway or route, or to any subpopulation. (p. 97) EPA provided no explanation other than to assert that exposure would only occur "in the event the packaged raw material or formulated products are damaged, resulting in the potential release of HBCD." (p. 97) EPA provided no citation for this assumption, or more generally to support its conclusion that no exposure will occur during the distribution of HBCD.

Consumer Exposures: In regards to consumer exposures, EPA states it plans to look at most exposure pathways for the conditions of use it is not excluding from the risk evaluation. Notably, EPA acknowledges that consumer articles containing HBCD have long service lives and that the chemical is present during the entire useful life of the article. (p. 37) This means that the potential for consumer exposure to HBCD in electronic products and children's products, uses that EPA has chosen to ignore as "legacy," will also continue to persist. EPA will also conduct no further analysis on consumer exposure (including to children) to building and construction materials that contain HBCD, specifically insulation in residential buildings. (p. 99) This exclusion is on the basis of EPA's assertion that consumers (including children) are not likely to be in direct contact with insulation; however, EPA has not provided evidence demonstrating that children are unlikely to come into contact with insulation and, for example, place it in their mouths and hence that this activity is not reasonably foreseen. For example, children living in substandard housing where insulation may be exposed may well be exposed in this very manner.

General Population Exposures: Unlike in many of the other problem formulations, EPA states it will generally look at exposures to the general population for HBCD. (p. 38) However, EPA will only do so for exposures it has not excluded. As mentioned earlier, because EPA's information indicates that many of the uses of HBCD have only recently ceased, it is unclear how EPA will decide whether an exposure to the general population is from what it considers a "condition of use" or from a legacy use.

F. EPA's stated commitment to addressing background levels does not remedy EPA's multiple exclusions.

EPA states that:

> For HBCD, EPA plans to analyze background levels for indoor dust, indoor air, ambient air, surface water, sediment, soil, dietary food sources, aquatic biota, and terrestrial biota. EPA has not yet determined the background levels in these media or how they *may* be used in the risk evaluation. (pp. 56-57, emphasis added)

EPA similarly repeats its intention to look at background levels in its Exposure Conceptual Model (pp. 99-105). In the case of HBCD, which EPA has stated is ubiquitous in the environment, EPA *must commit* to considering background levels in the risk evaluation in order to account for exposures not able to be linked to a specific condition of use of HBCD.

However, the consideration of background levels does not provide a justification for EPA's exclusions, including its exclusions of so-called legacy uses or other past uses, from the scope of this risk evaluation. For the reasons already discussed in these comments (see Section 4.A), EPA needs to include those uses and associated exposures and directly evaluate them in its risk evaluation.

31. EPA has failed to address how it plans to fill the numerous information gaps identified in the HBCD problem formulation.

In the HBCD problem formulation two categories of information gaps can be identified. The first category includes instances where there is little to no data at all available to EPA.

For example, EPA admits that "little is known" about the recycling of foam products containing HBCD. (p. 28) EPA's scant knowledge about the recycling of foam products is problematic because EPA states elsewhere in the problem formulation that the use of HBCD in foam "accounted for 95% of all HBCD applications in the past decade," (p. 27), and that "most insulation containing HBCD is still in place." (p. 28) Despite this potentially large source of exposure, EPA offered no plan to develop additional information. EPA must identify steps it will take to address this information gap.

EPA also admitted that there is "limited information available" regarding the mild irritation and sensitizing potential of HBCD. (p. 43) Even though EPA recognized the uncertainty related to this hazard, EPA did not indicate (as it did in other instances) that this hazard would be subject to further evaluation. EPA must commit to further developing and analyzing information about these potential hazards.

EPA also stated that it would "try to obtain" additional information about how HBCD is used in automobile replacement parts. (p. 27) As this use is one of the few that EPA has not yet excluded, and one that companies have acknowledged is an ongoing use, EPA must lay out a clear plan for acquiring additional information about it. Stating that it will merely "try" to collect additional information is not sufficient.

EPA also stated that where information was not available, rather than require the development or submission of the information, it would rely on models. In particular, EPA stated that:

> If measured values resulting from sufficiently high-quality studies are not available (to be determined through the systematic review process), chemical properties will be estimated using EPI Suite, SPARC, and other chemical parameter estimation models. Estimated fate properties will be reviewed for applicability and quality. (p. 60)

EPA's reliance on models as a first resort raises concerns over the resulting uncertainty associated with the conclusions it draws. It also flies in the face of the enhanced information authorities EPA was provided under the reforms made to TSCA in 2016 and raises the question once again as to why EPA refuses to use these authorities even in the face of significant information gaps.

Additionally, "EPA was not able to identify release scenarios corresponding to several conditions of use (e.g. recycling, construction and demolition) of products containing HBCD." (pp. 59, 63) This

information gap is concerning because, after EPA's numerous exclusions of conditions of use, these three conditions of use make up a significant part of the remaining scope (only eight conditions of use were identified as included in the problem formulation, p. 29). That "EPA *may* conduct industry outreach efforts, or perform supplemental, targeted literature searches to better understand the process steps involved" (p. 59, emphasis added) is not a sufficient means to address this critical data gap, nor is EPA's vague and caveated reference to outreach efforts entirely convincing. EPA must firmly commit to filling this information gap.

A second category of information gaps involves areas of uncertainty in hazard data. EPA has frequently indicated that certain effects are unknown, inconsistent, or variable. For instance:

1. "For female reproductive effects, there is some rodent evidence that HBCD may alter fertility and pregnancy outcomes as well as reduce the number of mature and developing follicles in the ovary; however, effects on reproductive organ weight are *inconsistent*." (p. 43, emphases added)
2. "There is *mixed* epidemiological data on developmental toxicity of HBCD, while animal toxicity studies suggest that early life exposure to HBCD at high doses can affect various developmental outcomes, including reduced offspring viability, decrements in pup weight and alterations in eye opening." (p. 43, emphasis added)
3. "Overall, immunological effects from HBCD exposure are *variable* and *inconsistent* across studies for endpoints such as immune organ weights, hematology or histopathology (U.S. EPA, 2014d), and its relevance to the risk evaluation will require further evaluation." (p. 43, emphases added)
4. "Although the current data does not appear to provide sufficient evidence that HBCD is carcinogenic, EPA will further evaluate genotoxicity and other cancer hazards in the risk evaluation as part of a systematic review." (p. 43)
5. "Data sources associated with indoor exposure pathways have not been comprehensively evaluated, quantitative comparisons across pathways or in relation to toxicity thresholds are not yet available." (p. 65)
6. "EPA has grouped the scenarios into 8 representative release/exposure scenarios of which 7 will be further analyzed. EPA was *not able to identify* occupational scenarios corresponding to some conditions of use (e.g. recycling, construction and demolition)." (p. 64, emphasis added) Notably, these uses include a considerable portion of the remaining conditions of use that impact workers.

It does not appear that EPA has developed any concrete plan to address these data gaps. EPA must develop and carry out a plan for filling these gaps.

In some cases, EPA specifically indicated that it may choose not to take any steps to address a data gap. For instance, "depending on available information," EPA may analyze exposure to occupational non-users (persons who do not directly handle the chemical but perform work in an area near where the chemical is present)." (p. 36) EPA also states that:

> If sufficient toxicity studies *are not identified* in the literature search to assess risks from dermal and inhalation exposures, then a route-to-route extrapolation from oral toxicity studies would be needed to assess systemic risks from dermal or inhalation exposures. (p. 73, emphasis added)

EPA was given broad authority under TSCA to obtain information, *see* 15 U.S.C. §§ 2603, 2607; therefore, if EPA is lacking needed information, it must use its authorities to obtain that information, rather than avoid evaluating potential exposures, especially when the information gap involves exposures to a potentially exposed or susceptible subpopulation.

32. EPA's problem formulation contains several statements relating to confidential business information (CBI) that are or may be inconsistent with its authorities and obligations under TSCA.

The life cycle diagram for HBCD has not been fully disclosed to the public because the specific production volumes provided in the 2016 CDR were "claimed as confidential business information." (p. 30) It has been two years since EPA collected that information, and almost two years since EPA announced that HBCD would be one of the first ten chemicals reviewed under section 6, yet EPA has apparently not reviewed those CBI claims or prioritized its review of HBCD claims despite the ongoing risk evaluation. EPA's failure to conduct the timely reviews TSCA mandates of CBI claims made in submissions under the CDR is resulting in the public being precluded from understanding the conditions of use of this chemical. This information is critical to understanding the impacts of EPA's exclusions and hence such claims should immediately be reviewed (and the determinations made public).

It is also curious that the 2015 production volume remains confidential even though EPA is excluding a host of uses that were ongoing at that time (e.g., use in EPS resin and use in HIPs). (p. 30) If those companies have communicated to EPA that manufacture for some of those uses from 2015 are no longer ongoing, (p. 21), why are their site-specific volumes still confidential and the national production volume still withheld, since it allegedly no longer reflects the "ongoing" production of HBCD in the United States? EPA must ensure that these claims meet the applicable CBI requirements under TSCA.

EPA also states that EPA "may consider any relevant CBI information in the risk evaluation in a manner that protects the confidentiality of the information from public disclosure." (p. 56) This statement ignores the major changes made to the CBI provisions of TSCA section 14. Companies must substantiate most claims for CBI protection and EPA must review many of them within 90 days of submission of the information. Any claim that does not meet all applicable requirements cannot be protected from disclosure.

33. The review of HBCD under TSCA should utilize all of the materials developed by the IRIS program before the assessment was transferred to the TSCA program.

In early 2018, it appears that EPA's Office of Research and Development (ORD) stopped its assessment of HBCD. In email correspondence between ORD and the Office of Chemical Safety and Pollution

Prevention (OCSPP),[151] ORD indicated that it had developed a number of materials in the latter half of 2017 that were not yet incorporated into the Toxicological Review. These include:

- Data extraction of animal toxicology studies into HAWC and QC;
- Study evaluation of both epidemiology and animal toxicology studies in HAWC;
- Data visualization in HAWC (including development of an exposure-response array visualization option for the HAWC software, which was used to develop new HBCD arrays);
- Literature screening of new studies and discussions of how to incorporate them into the draft;
- Development of an IRIS assessment protocol and review by agency partners;
- Preliminary development of evidence profile tables that reflect evidence integration for each hazard;
- Discussions of within- and across-stream evidence integration as well as hazard conclusions using the structured framework in the IRIS Handbook; and
- A revised structure for the Toxicological Review, primarily reflecting changes in presentation of the methods and results of the systematic review.

ORD also indicated that an RfD had been derived, and that the systematic review documents were also available.

Because, according to the email, none of these items were provided to OCSPP in early 2018, EPA should ensure that these materials have been obtained and incorporated by OCSPP into its risk evaluation for HBCD. Notably, the problem formulation only states that EPA has looked at the Preliminary Materials for the IRIS Toxicological Review of HBCD from 2014, (pp. 42, 70), which appears to be distinct from the materials ORD referenced in its letter. Moreover, since additional emails between ORD and OCSPP suggest that the frameworks and systematic reviews for HBCD differed between the two offices, it is especially critical that OCSPP look closely at the materials already derived by ORD.[152] EPA should then explain any deviations from the ORD materials.

34. EPA must look at exposures and hazards to all aquatic organisms, including marine mammals.

EPA states that it will analyze hazards of HBCD to "aquatic organisms including fish, aquatic invertebrates, aquatic plants, and sediment invertebrates" but does not mention aquatic organisms that are not fish, such as marine mammals. (p. 42) Although this list is more comprehensive than in other problem formulations (e.g., TCE), the failure to include marine mammals is a significant oversight in regards to HBCD. Numerous studies in EPA's search results for HBCD indicate that HBCD has been

[151] Available through FOIA at https://www.foiaonline.gov/foiaonline/action/public/submissionDetails?trackingNumber=EPA-HQ-2018-004651&type=request (the documents are currently not available through the updated FOIA, but the commenter has a copy if requested).
[152] Available through FOIA at https://www.foiaonline.gov/foiaonline/action/public/submissionDetails?trackingNumber=EPA-HQ-2018-004651&type=request (the documents are currently not available through the updated FOIA, but the commenter has a copy if requested).

found in increasing levels in marine mammals.[153] EPA must comprehensively consider all relevant aquatic organisms in its assessment of exposures to HBCD via contaminated surface water.

Moreover, unlike other problem formulations where EPA has calculated a concentration of concern in surface water, (e.g., see the problem formulation for 1-bromopropane, pp. 42-43), EPA has not done so for HBCD. Instead EPA stated that:

> The aquatic environmental hazard studies *may* be used to derive acute and chronic concentrations of concern (COC) for mortality, behavioral, developmental and reproductive or other endpoints determined to be detrimental to environmental populations. Depending on the robustness of the evaluated data for a particular organism (*e.g.* aquatic invertebrates), environmental hazard values (e.g. ECx/LCx/NOEC/LOEC, etc.) *may* be derived and used to further understand the hazard characteristics of HBCD to aquatic species. (p. 69, emphases added)

EPA must commit to collecting the information necessary to derive these values; stating that they may not do so depending on the "robustness" of the data is not a valid reason.

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[153] *See, e.g.*, Hoguet, J., et al., *Spatial and temporal trends of persistent organic pollutants and mercury in beluga whales (Delphinapterus leucas) from Alaska*, SCI. OF THE TOTAL ENV'T 449: 285-294 (2013), http://dx.doi.org/10.1016/j.scitotenv.2013.01.072; Montie, EW, et al., *Brominated flame retardants and organochlorine contaminants in winter flounder, harp and hooded seals, and North Atlantic right whales from the Northwest Atlantic Ocean*, MAR. POLLUT. BULL. 60: 1160-1169 (2009), http://dx.doi.org/10.1016/j.marpolbul.2010.04.002; Lam, JC, et al., *Temporal trends of hexabromocyclododecanes (HBCDs) and polybrominated diphenyl ethers (PBDEs) and detection of two novel flame retardants in marine mammals from Hong Kong, South China*, ENVTL. SCI. TECHNOL. 43: 6944-6949 (2009), http://dx.doi.org/10.1021/es901408t.

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Comments on 1,4-Dioxane

35. EPA has excluded or failed to sufficiently analyze numerous conditions of use and exposure pathways for 1,4-dioxane.

A. EPA has inappropriately excluded all consumer uses and all contamination of industrial, commercial and consumer products.

EPA asserts that it "did not find evidence of any current consumer uses for 1,4-dioxane and is excluding consumer uses from the scope of the risk evaluation" and that "contamination of industrial, commercial and consumer products are *not intended conditions of use* for 1,4-dioxane and will not be evaluated." U.S. EPA, Problem Formulation of the Risk Evaluation for 1,4-Dioxane at p. 18 (emphasis added) (May 2018), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0723-0064. For support, EPA cites its earlier scope document. *See* 1,4-Dioxane, Scope, Docket ID: EPA-HQ-OPPT-2016-0723.

In our comments on the scope document, EDF already commented at length on the illegality of these exclusions; those comments are incorporated here by reference. EDF Comments on Ten Scopes under the Toxic Substances Control Act, https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0743-0069. In brief, EPA's position that it can ignore known and foreseeable conditions of use of a chemical violates the text of the law. "Conditions of use" expressly includes "the circumstances *** under which a chemical substance is intended, known, or reasonably foreseen to be to be manufactured, processed, distributed in commerce, used, or disposed of." 15 U.S.C. § 2602(4). Congress expressly chose to define "conditions of use" broadly to include not only "intended," but also "known" or "reasonably foreseen" manufacture, processing, distribution, use, and disposal. 15 U.S.C. § 2602(4). Disregarding chemical substances such as 1,4-dioxane that are present in products as impurities or byproducts because they are not "intended" essentially reads the other two scenarios out of the statute. This exclusion will result in a deficient and erroneous evaluation and determination of the chemical's risks.

EPA's scope document identified numerous products that "potentially contain[] 1,4-dioxane as a residual contaminant, including paints, coatings, lacquers, ethylene glycol-based antifreeze coolants, spray polyurethane foam, household detergents, cosmetics/toiletries, textile dyes, pharmaceuticals, foods, agricultural and veterinary products," as well as "magnetic tape and adhesives." *See* 1,4-Dioxane, Scope at p.21, Docket ID: EPA-HQ-OPPT-2016-0723. And in EPA's 2015 Problem Formulation and Initial Assessment for 1,4-dioxane, EPA stated:

> EPA/OPPT concludes that exposure to consumers can result from the use of soaps and detergents and other products that contain 1,4-dioxane as a contaminant. Adult women who use multiple cosmetics and cleaning products are likely the most exposed population as determined in the Canada assessment.[154]

[154] *See* U.S. EPA, *TSCA Work Plan Chemical Problem Formulation and Initial Assessment, 1,4-Dioxane, CASRN: 123-91-1* at 28 (Apr. 2015), https://www.epa.gov/sites/production/files/2017-06/documents/14_dioxane_problem_formulation_and_intial_assessment.pdf.

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Bizarrely, EPA nonetheless concludes in its problem formulation that it "did not find evidence of any current consumer uses for 1,4-dioxane." (p. 18)[155] As discussed in detail in our earlier comments, these products are known and reasonably foreseen conditions of use leading to exposures to 1,4-dioxane, and EPA's decision to ignore them when analyzing whether this chemical presents an unreasonable risk is arbitrary and capricious. EPA must analyze these conditions of use in the risk evaluation.

B. Major deficiencies abound in EPA's assertion that exposures to 1,4-dioxane falling under other legal jurisdictions are adequately managed.

We have discussed earlier (see Section 5) the many legal flaws in EPA's assertion that it can ignore exposure pathways that fall under other EPA authorities and assume they "adequately assess and effectively manage" any risks. EPA's 1,4-dioxane problem formulation also contains many technical and scientific flaws or inaccuracies. To illustrate, we provide below some specific comments on unsupported or insufficiently supported statements in the document, as examples of EPA's failure to adequately justify on scientific grounds the sweeping exposure pathway exclusions it has proposed.

Air emissions: In seeking to justify its exclusion of exposures from air emission pathways, EPA states:

> 1,4-Dioxane is a HAP. EPA has issued a number of technology-based standards for source categories that emit 1,4-dioxane to ambient air and, *as appropriate*, has reviewed, *or is in the process of reviewing remaining risks.* Because stationary source releases of 1,4-dioxane to ambient air are adequately assessed and any risks effectively managed when under the jurisdiction of the CAA, EPA does not plan to evaluate emission pathways to ambient air from commercial and industrial stationary sources or associated inhalation exposure of the general population or terrestrial species in this TSCA evaluation. (p. 43, emphases added)

In the Appendix, EPA merely provides a list of technology-based standards for certain source categories. EPA provides no analysis whatsoever as to: the extent to which the standards cover the full range of stationary sources of this chemical; the extent and magnitude of releases of the chemical allowed under each of the standards; the duration, intensity, frequency, and number of exposures resulting from those allowable emissions (as required under TSCA section 6(b)(4)(F)(iv)); or any other factors that would be necessary to analyze and determine the extent and nature of potential risk allowed under the standards. EPA has not acknowledged, let alone analyzed, the overall risks to the general population or to vulnerable subpopulations due to the combination of exposures arising from the various sources for

[155] Equally bizarrely, EPA states: "The 1,4-dioxane life cycle diagram (Figure 2-1) indicates that no uses of 1,4-dioxane were identified in consumer products. *EPA did not receive data, information or comments that informed a change was necessary to the scope.*" (p. 41, emphasis added) This statement is, of course, demonstrably false. EPA's own scope document identifies numerous uses of 1,4-dioxane in consumer products, as did EDF's and, no doubt, many others' comments.

which standards exist, not to mention additional emission sources not subject to any standard. EPA has made no attempt to reconcile any such risk with that allowed under TSCA.

In the absence of such analyses, there is no basis whatsoever for EPA to assert that air releases of this chemical have been adequately assessed or that any risks have been effectively managed under TSCA's standards.

EPA offers only a vague claim that EPA "as appropriate, has reviewed, or is in the process of reviewing remaining risks." No specifics as to the status of or timeline for such reviews have been provided, and no indication is made as to when and on what basis such reviews are deemed "appropriate." Nor have the results of any such reviews that have been completed been provided, let alone analyzed in the context of TSCA's requirements.

Drinking water exposures: In seeking to justify its exclusion of drinking water pathways, EPA states:

> EPA's Office of Water has established a Health Advisory level of 35 µg/L (which corresponds to a 1 in ten thousand lifetime cancer risk) for 1,4-Dioxane. (p. 43)

This statement is highly misleading as it misconstrues the context and purpose of Health Advisories. Here is what the Office of Water's own Health Advisory 2018 compilation states:

> HAs [Health Advisories] are intended to protect against *noncancer effects*. The 10^{-4} Cancer Risk level provides information concerning cancer effects.[156]

EPA's own November 2017 Fact Sheet on 1,4-dioxane – never mentioned in the problem formulation – cites the 1,000-fold lower level of 0.35 ug/L that corresponds to EPA's typical cancer risk protection goal for general populations of 10^{-6} (a 1-in-one-million lifetime cancer risk). It also shows that most states have guidelines far below 35 ug/L.[157]

EPA's problem formulation goes on to state:

> 1,4-Dioxane is also currently listed on EPA's Fourth Contaminant Candidate List (CCL 4) and was subject to occurrence monitoring in public water systems under the third Unregulated Contaminants Monitoring Rule (UMCR 3). Under UMCR 3, water systems were monitored for 1,4-dioxane during 2013-2015. Of the 4,915 water systems monitored, 1,077 systems had detections of 1,4-dioxane in at least one sample. None of the systems measured levels greater than the Health Advisory level, *however, 341 systems (6.9%) had results at or above 0.35 µg/L (which corresponds to a 1 in a million-*

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[156] U.S. EPA, *2018 Edition of the Drinking Water Standards and Health Advisories Tables* at p. iii (Mar. 2018), https://www.epa.gov/sites/production/files/2018-03/documents/dwtable2018.pdf (emphasis added).

[157] U.S. EPA, *Technical Fact Sheet 1,4-dioxane* at 3-4 (Nov. 2017), https://www.epa.gov/sites/production/files/2014-03/documents/ffrro_factsheet_contaminant_14-dioxane_january2014_final.pdf.

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> *lifetime cancer risk).* In accordance with EPA-OW's process, 1,4-dioxane is *currently being evaluated* under the fourth Regulatory Determination process under SDWA.
>
> Hence, because the drinking water exposure pathway for 1,4-dioxane is being addressed under the regular analytical processes to identify and evaluate drinking water contaminants of potential regulatory concern for public water systems under SDWA, EPA does not plan to include this pathway in the risk evaluation for 1,4-dioxane under TSCA. (p. 43, emphasis added)

This excerpt contains misleading or inaccurate statements or implications. First, by EPA's own admission, the CCL is "a list of *unregulated* contaminants" (p. 43; emphasis added). Numerous additional steps would be needed to actually regulate 1,4-dioxane under SDWA, which have not been taken. The vague statement that the chemical is "currently being evaluated" – with no specification of what outcomes may result or any timeline for further action toward regulation – provides no basis for EPA's assertion that its risks are being "adequately assess[ed] and effectively manage[d]."

Second, EPA again erroneously states that 35 ug/L is the Health Advisory level, and then uses that level to assert there are no exceedances. In fact, as EPA notes, nearly 7% of public water systems – serving 7 million Americans – exceed the risk level representing acceptable risk to the general population.

EPA's decision to ignore such clearly significant levels of exposure and risk, and to refuse to evaluate their contribution to the overall risks of this chemical, is unconscionable.

Ambient water pathways: EPA's problem formulation states: "EPA has not developed CWA section 304(a) recommended water quality criteria for the protection of aquatic life for 1,4-dioxane. ... Currently, only one state (Colorado) includes human health criteria for 1,4-dioxane in their water quality standards and none include aquatic life criteria for 1,4-dioxane. As a result, this pathway will undergo aquatic life risk evaluation under TSCA (see Section 2.5.3.2)." (p. 44)

EPA never indicates that it has also *not* set a recommended water quality criterion for human health for this chemical. Yet inexplicably, it appears EPA plans to exclude ambient water pathways from the risk evaluation of human health risks to the general population. EPA has provided no justification for this exclusion.

In addition, despite EPA's statement (cited above) that "this pathway will undergo aquatic life risk evaluation under TSCA" (p. 44), Appendix E of the problem formulation contradicts that statement, indicating that aquatic species exposure via water will not be subject to any further analysis.

In sum, EPA must analyze these exposure pathways in the risk evaluation in order for it to be consistent with the best available science and reasonably available information.

C. EPA has insufficiently justified many of its decisions not to include known or potential exposures or conduct further analysis, and has prematurely concluded various exposures present no significant risk.

EPA's 1,4-dioxane problem formulation contains many rushes to judgment, with EPA all but concluding there is no unreasonable risk from certain exposures, based on little analysis and with no indication that it intends to revisit those exposures or risks in combination with those it does intend to analyze further. To illustrate, we provide below some specific examples.

Risks to aquatic invertebrates and aquatic plants: With little analysis and based on limited data, EPA asserts that "[m]easured and estimated levels of 1,4-dioxane in the environment are sufficiently below the acute and chronic aquatic COCs [concentrations of concern]," plans no further analysis, and implies it has concluded that any associated risks can be ignored (p. 41). Yet:

- EPA's predicted concentrations in surface water for acute and chronic scenarios are up to 58% and 40% of the COCs, leaving little room for error.
- Elsewhere, EPA acknowledges "[T]here are relatively fewer data available on 1,4-dioxane levels in surface water," (p. 28), indicating a data gap that EPA apparently will do nothing to address.
- EPA implies that its calculations of COCs are conservative at least in part because of its use of assessments factors (pp. 29, 70, 81). The use of such factors is not conservative: They account for *real-world sources of variability as well as database limitations*, and cannot be construed as "safety factors" that yield conservative estimates.[158] As EPA states: "The application of AFs [assessment factors] provides a lower bound effect level that would likely encompass more sensitive species not specifically represented by the available experimental data. AFs are also account for differences in inter- and intra-species variability, as well as laboratory-to-field variability." (p. 70)
- EPA's calculated acute COC is inconsistently reported. In the text, it is listed as 59,800 ppb (p. 35), while in Appendix C it is listed as 20,000 ppb (p. 70). EPA's modeling of surface water concentrations includes assumptions that are not necessarily conservative, despite EPA's claims to the contrary.

For example, EPA points to the surface water modeling assumption that "[w]astewater treatment removal is assumed to be 0% for this exercise" (p. 29); yet its own modeling of wastewater treatment removal efficiency using EPISuite STP module indicates removal rates will be very low, on the order of 2% (p. 24). Far from being a conservative assumption, this use of 0% is a reasonable conclusion based on the available data. Despite a promised "full table of results, see Appendix E" (p. 29), that table provides only EPA's conclusions and none of its analysis.

[158] *See* section 14 of these comments.

EPA's current analysis is incoherent and unexplained. EPA must obtain additional information on exposure through this pathway as well as hazard, and EPA must prepare a scientifically valid analysis of this pathway.

Risks to sediment organisms: EPA states: "While no ecotoxicity studies were available for sediment organisms, the toxicity of 1,4-dioxane to sediment invertebrates is expected to be similar to the toxicity to aquatic invertebrates." (p. 42) EPA provides no basis for this assertion of expected similar toxicity. This is a clear data gap that EPA should have filled, or should now move to fill, rather than resort to such hand-waving to dismiss a potential risk it has not examined.

Occupational exposures: Occupational exposures appear to be the only exposures to 1,4-dioxane EPA will further analyze. But how it will sufficiently do so is far from clear. Below we cite examples of statements that are vague at best as to their intent or implications for EPA's occupational exposure assessment.

EPA states: "EPA will evaluate applicable regulatory and non-regulatory exposure limits." (p. 48) The meaning of this statement is not at all clear; what does it mean that EPA will "evaluate" such limits? Will it do so to determine their adequacy to address risks to workers? What assumptions will EPA make as to their extent of applicability to various exposure sources, or the extent of compliance with them? EPA needs to provide far more detail than it has. See section VI for more on this concern.

EPA states: "For conditions of use where data are limited or not available, review existing exposure models that may be applicable in estimating exposure levels." (p. 48) EPA appears to acknowledge that clear exposure data gaps exist, yet avoids any mention of using its authorities to fill the gaps. TSCA Section 4 provides EPA with clear authority to require monitoring or other exposure studies to be conducted, while section 8 provides authority to require reporting of existing studies or data. Yet EPA merely indicates it will review existing models, begging the question as to the adequacy or reliability of the models to address the identified gaps, and what EPA will do if the available models are insufficient.

EPA states: "During distribution, 1,4-dioxane is contained in closed systems (e.g. drums, pails, bottles) so *releases and exposures are not expected.*" (p. 37; emphasis added) This blanket assertion is made with absolutely no supporting analysis or data, either documenting the extent to which the identified "closed systems" are actually used, or the extent to which they are in fact "closed" and lead to no releases or exposure whatsoever, as EPA asserts. Even on their face, the examples raise many questions. For example: Are drums or bottles never open? How is a pail a "closed system"?

EPA states: "EPA reviewed the potential for occupational exposures associated with subcategories of conditions of use where a mist may be generated. *EPA determined that most subcategories will not produce a mist during their typical use and, for these, EPA concludes that exposure to 1,4-dioxane would be negligible and does not plan further analysis.*" (p. 37, emphasis added) EPA appears to have conducted no analysis, at all, let alone any "further analysis." It provides no supporting analysis or data to support this sweeping assertion. Yet EPA has drawn an apparently final conclusion not to be revisited that exposure is "negligible."

EPA states it will:

> 4) Consider and incorporate applicable engineering controls and/or personal protective equipment into exposure scenarios. EPA will review potential data sources on engineering controls and personal protective equipment as identified in Table 2-10 to determine their applicability and incorporation into exposure scenarios during risk evaluation." (p. 49)

EPA provides no indication as to how it will "consider and incorporate" such controls or equipment into its exposure scenarios. Myriad questions arise. What assumptions will be made as to their extent of use, their efficacy, etc.? Limitations on the extent of use and the efficacy of workplace controls, especially for PPE, have been illuminated by both OSHA and EPA. EDF discusses this issue at greater length in section 13 of these comments.

EPA's vague and unexplained statements about its planned analyses raise serious concerns and often lack any empirical basis. EPA must analyze occupational exposures based on the best available science, and EPA must use its information authorities to obtain reasonably available information about these exposures.

General population exposures: EPA states that it "does not expect to consider and analyze general population exposures in the risk evaluation for 1,4-dioxane." (p. 49) Yet its own analyses point to the clear potential for such exposures. Below are some examples.

EPA states:

> Indoor air exposures may occur from infiltration from ambient air or emissions from tap water during activities such as showering and bathing. Based on the relatively high water solubility and relatively low Henry's law constant for 1,4-dioxane, EPA expects that volatilization would be low for many indoor uses. However, increased water temperature during bathing and showering can increase volatilization. (p. 31)

In addition to exposure to 1,4-dioxane contaminated tap water used for showering or bathing, use of products containing 1,4-dioxane especially in warm or hot water could also lead to exposures. This would include personal care products like shampoo or soap (some of which may not fall under TSCA jurisdiction) but also various cleaning, laundry or related products that could or would be used in hot or warm water. EPA must analyze exposures to the general population, including exposures through water and products.

EPA states: "1,4-Dioxane has also been detected in landfill leachate (ATSDR, 2012)." (p. 28) Yet it intends to wholly exclude such exposures based on presumed adequate management under federal or state law, absent any analysis demonstrating this. The fact that 1,4-dioxane is present in liquids leaching from landfills suggest that it may be coming from consumer products containing it – yet another demonstration of how arbitrary EPA's decision is to ignore exposures associated with consumer use of products containing the chemical.

36. EPA statements raising questions about the available science identifying health risks are vague and insufficiently supported.

EPA states:

> EPA expects to use these previous analyses [including the IRIS assessment] as a *starting point for identifying key and supporting studies* to inform the human health hazard assessment, including dose-response analysis. (p. 35, emphasis added)

Is EPA planning to use these prior assessments *only* for the purpose of identifying studies? If so, on what basis is it rejecting the hazard assessments themselves? If EPA now believes there are flaws or shortcomings in those earlier assessments, it should clearly identify them and provide the basis for its beliefs.

EPA should not lightly disregard EPA's existing peer-reviewed IRIS assessment for 1,4-dioxane, including the hazard values which the agency has relied on in the past. EPA must identify and explain any decision to deviate from these values, as well as the scientific basis for such deviation.

EPA refers to "key" and "supporting" studies, but the meaning of these descriptors is entirely unclear. EPA must explicitly define the meaning of these terms and their implications with regard to the agency's approach to systematic review and risk evaluation.
EPA states:

> Human health hazards from acute and chronic exposures will be identified by evaluating the human and animal data that *meet the systematic review data quality criteria* described in the Application of Systematic Review in TSCA Risk Evaluations document (U.S. EPA, 2018a). Data quality evaluation will be performed on key studies identified from the IRIS assessments (U.S. EPA, 2013b, 2010), the *TSCA Work Plan Problem Formulation and Initial Assessment* (U.S. EPA, 2015c) and studies published after 2010 (oral) and 2013 (inhalation) that were captured in the comprehensive literature search. *Hazards identified by studies meeting data quality criteria* will be grouped by routes of exposure relevant to humans (oral, dermal, inhalation) and by cancer and noncancer endpoints. (p. 51, emphases added)

EPA has not explained, either here or in its systematic review document, what it means for data or studies to "meet the systematic review data quality criteria." Moreover, this language suggests EPA will apply its criteria in a black-or-white manner: a study is either in or out. How is this consistent with the statute's requirement that EPA take a weight-of-evidence approach? How is it consistent with the scientific standards in TSCA section 26(h), which require EPA to consider the "extent" or "degree" to which various factors characterize information, methods, models, etc. – which does not support the black-or-white approach EPA appears to intend to apply.

EPA states: "Some data support a non-linear MOA [mode of action] for liver tumorigenesis." (p. 36) Notably, EPA has provided no data and citations to support this contention.

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EPA may have in mind work published by Dr. Michael Dourson, who has argued for a non-linear MOA for 1,4-dioxane in work sponsored by PPG Industries, a major user of the chemical.[159] Dourson argued for a far less health-protective standard, about 1000-fold weaker, than the value in EPA's IRIS assessment indicative of an increased cancer risk of 10^{-6}. Scientists employed by the Michigan Department of Environmental Quality[160] and the New Jersey Department of Environmental Protection[161] reviewed Dourson's work on this chemical and found it sorely lacking on scientific grounds. These and other states (including Colorado and Massachusetts) have rejected a non-linear MOA for 1,4-dioxane and have set their standards and guidelines at levels commensurate with the IRIS value.

EPA states: "Human occupational studies into the association between 1,4-dioxane exposure and increased cancer risk are inconclusive because they are limited by small cohort size and a small number of reported cancer cases." (p. 36) EPA has provided no reference to said occupational studies or indicated why they are "inconclusive." Further, EPA appears to have identified a data gap, yet makes no mention of any next step to address the gap. Why not?

37. EPA has not identified all relevant potentially exposed or susceptible subpopulations.

At the end of its section on Human Health Hazards (section 2.4.2.3), EPA states:

> In developing the hazard assessment, *EPA will analyze available data to ascertain whether some human receptor groups may have greater susceptibility than the general population* to the chemical's hazard(s). (p. 36)

In setting the scope of a problem formulation, TSCA requires that EPA identify "potentially exposed or susceptible subpopulations," 15 U.S.C. § 2605(b)(4)(D), including those that "due to ... greater *susceptibility* ... may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture." 15 U.S.C. § 2602(12) (emphasis added). This omission of specific subpopulations stands in contrast to the analogous subsection under Human Exposure (p. 32), where EPA identified specific subpopulations that "EPA expects to consider in the risk evaluation due to their greater exposure." This needs to be remedied.

In the analogous section under Human Exposure (p. 32), EPA also should include consumers and adult women who use multiple cosmetics and cleaning products as potentially exposed or susceptible subpopulations, given EPA's prior identification of those subpopulations as particularly likely to be

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[159] Michael Dourson, et al., *Mode of action analysis for liver tumors from oral 1,4-dioxane exposures and evidence-based dose response assessment*, 68:3 REGULATORY TOXICOLOGY & PHARMACOLOGY 387-401 (Apr. 2014), https://www.ncbi.nlm.nih.gov/pubmed/24491968.

[160] *See* Mich. Dep't of Envtl. Quality, Toxics Steering Group, 1,4-Dioxane Subcomm., *Review of a 1,4-Dioxane Presentation by Michael Dourson, Ph.D. on October 8, 2013* (Feb. 2015), https://www.michigan.gov/documents/deq/deq-aqd-toxics-14-DioxaneTSG_Report_2015_487415_7.pdf.

[161] *See* N.J. Dep't of Envtl. Protection, *Response to Public Input on Draft Interim Ground Water Quality Criteria and Draft Interim Practical Quantitation Levels for Eleven Chemicals* at pp. 11-17, https://www.state.nj.us/dep/dsr/supportdocs/11-chemicals-response.pdf.

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exposed; see Section 35.A. Workers likely to be using industrial or commercial products contaminated with 1,4-dioxane should also be identified.

38. EPA's problem formulation contains statements relating to confidential business information (CBI) that are or may be inconsistent with its authorities and obligations under TSCA.

EPA states: "EPA may consider any relevant CBI in the risk evaluation in a manner that protects the confidentiality of the information from public disclosure." (p. 47) This statement ignores the major changes made to the CBI provisions of TSCA section 14. Companies must substantiate most claims for CBI protection and EPA must review many of them within 90 days of submission of the information. Any claim that does not meet all applicable requirements cannot be protected from disclosure.

Health and safety studies are expressly not eligible for protection as CBI under TSCA, subject only to two very narrow exceptions. *See* 15 U.S.C. § 2613(b)(2). All such information not subject to the exceptions needs to be made public.

Comments on DCM

39. EPA should promptly finalize its proposed ban of DCM in paint strippers.

On May 10, 2018, EPA committed[162] to finalizing its proposed ban on all consumer and commercial uses (except for commercial furniture refinishing) of methylene chloride (also known as dichloromethane, DCM, and hereafter referred to as DCM) in paint and coating removal products. However, in the intervening three months (and counting), the agency has failed to uphold this commitment.

EDF incorporates by reference its comments on EPA's proposed rule to ban DCM for paint and coating removal.[163] EPA's 2014 DCM Work Plan risk assessment (hereafter "DCM risk assessment") and supplemental technical reports make clear that DCM, under the conditions of use subject to the proposed rule, presents an unreasonable risk of injury to the health of workers, consumers, and bystanders. These evaluations reflect the input from numerous and extensive peer reviews, incorporate the best available science, and apply a weight-of-the-scientific-evidence approach.

We urge EPA to promptly send a draft final rule to the Office of Management and Budget (OMB) and then expeditiously finalize this long-overdue ban.

40. EPA has excluded or failed to sufficiently identify and analyze relevant exposure pathways, hazards, and vulnerable subpopulations for DCM.

A. EPA has provided insufficient justification for its exclusion of certain activities from the risk evaluation.

EPA has excluded paint and coating removers, except for those used in commercial furniture refinishing, from the risk evaluation:

> While paint and coating removal falls under the conditions of use for methylene chloride, based on the intention to finalize the rulemaking the scenarios already assessed in the 2014 risk assessment these uses will not be re-evaluated and EPA will rely on the 2014 risk evaluation.

U.S. EPA, Problem Formulation of the Risk Evaluation for Methylene Chloride (Dichloromethane, DCM) at p. 21 (May 2018), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0742-0083.

EDF supports these intentions. However, EPA has placed these conditions of use into Table 2-2 (p. 21), which lists "Categories and Subcategories Determined Not to be Conditions of Use or Otherwise Excluded During Problem Formulation." EPA needs to clarify that the conditions of use subject to the proposed ban remain conditions of use of DCM. First, the ban has not been finalized, and until it has

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[162] News Release, U.S. EPA, EPA Announces Action on Methylene Chloride (May 10, 2018), https://www.epa.gov/newsreleases/epa-announces-action-methylene-chloride.

[163] EDF Comments on Regulation of Certain Uses under Toxic Substances Control Act: Methylene Chloride and N-Methylpyrrolidone, https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0231-0912.

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been and takes effect, these conditions of use are known conditions of use of DCM. Second, the ban as proposed was not absolute and included certain exemptions. Assuming the final rule retains these, EPA also must take into consideration any exposures remaining from the conditions of use allowed under the exemptions. Third, if EPA finalizes a rule that fails to completely ban consumer and commercial uses of these products (aside from commercial furniture refinishing) as proposed, it will need to consider remaining exposures in the current risk evaluation. Hence, the conditions of use subject to the rule must remain conditions of use in the DCM Problem Formulation.

Additionally, EPA has folded the conditions of use of DCM in paint and coating removal products associated with commercial furniture refinishing into the problem formulation; see Table 2-3, p. 25. This is not appropriate. While EPA deferred extending its ban to such conditions of use while it collected more information on alternatives, it indicated it would then move to propose a rule addressing those conditions of use as well.[164] EPA's 2014 risk assessment for DCM amply demonstrated that such conditions of use present unreasonable risk,[165] so there is no need for EPA to re-evaluate these conditions of use in the present risk evaluation. EPA should instead promptly move to propose a section 6 ban on DCM in paint and coating removal products associated with commercial furniture refinishing. It should be noted that EPA's stated need for more information on alternatives to DCM for these uses involves a *nonrisk factor* that TSCA precludes EPA from considering during the risk evaluation process. *See* 15 U.S.C. § 2605(b)(4)(A).

EPA has also excluded "Extraction solvent for oils, waxes, fats, spices and hops in agricultural chemical manufacturing and food processing" as a condition of use. Its rationale for doing so is that the uses meet the definition of a food additive under section 201 of the Federal Food, Drug, and Cosmetic Act. While it is reasonable to exclude such uses as a condition of use given that they do not meet the definition of a chemical substance under TSCA, EPA can and should consider exposures from such uses as contributing to background exposure that must be accounted for in determining the risk presented by DCM. It is nonsensical for EPA to ignore known background exposures to chemicals when it is charged with evaluating whether a chemical as a whole presents unreasonable risk.

There is clear precedent for accounting for exposures that fall outside those specified by the statute at hand. For example, the EPA's Office of Water routinely uses a Relative Source Contribution factor or a default of 20% of exposure from all sources to account for non-water sources of chemical exposure in establishing its drinking water standards and health advisories.[166] In other words, EPA accounts for non-

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

[165] U.S. EPA, *TSCA Work Plan Chemical Risk Assessment Methylene Chloride: Paint Stripping Use* at 118-19 (Aug. 2014), https://www.epa.gov/sites/production/files/2015-09/documents/dcm_opptworkplanra_final.pdf.

[166] U.S. EPA, *2018 Edition of the Drinking Water Standards and Health Advisories* (Mar. 2018), https://www.epa.gov/sites/production/files/2018-03/documents/dwtable2018.pdf.

water sources of exposure to the chemical even though they derive from exposure sources outside the authority to develop such standards and advisories under the Safe Drinking Water Act.

B. Exposure pathways are inappropriately excluded.

EPA's DCM Problem Formulation is largely irrational and often incoherent, with the agency both: 1) acknowledging many exposures that it later excludes, and 2) choosing to ignore exposure pathways with little or no explanation.

i) Major deficiencies and inconsistencies abound in EPA's assertion that exposures to DCM falling under other legal jurisdictions are adequately managed.

EPA has chosen to exclude all exposures to the general population based on the rationale that other statutes cover such exposures arising through air, water, and land releases. We have explained elsewhere why this is an illegal and unsound approach (see Section 5). However, it is also illogical, as the DCM Problem Formulation itself points to known exposures and potential risks to the general population from such exposures.

EPA explains that DCM is prevalent in environmental media:

> Due to its variety of uses and subsequent release to the environment, methylene chloride is present and measurable through monitoring in a variety of environmental media including ambient and indoor air, surface water and ground water, including sources used for drinking water supplies, sediment, soil and food products. (p. 35)

With regards to air, EPA provides the following evidence that DCM contamination in the air is widespread and likely increasing:

- DCM is "moderately persistent and is expected to be subject to atmospheric transport" (p. 33)
- 2,542,146 lbs of DCM was released into the air in 2015 based on Toxic Release Inventory (TRI) data. (p. 34)
- "Ambient air samples worldwide have shown measured levels of methylene chloride… Similarly, air concentrations in the continental U.S. between 2003 and 2014 showed either no trend or increasing levels of methylene chloride." (p. 35)
- "Between 1998 and 2006, >90% of all reported TRI releases of methylene chloride were air releases (U.S. EPA, 2014b) and levels of methylene chloride in the ambient air are widespread and shown to be increasing (Section 2.3.2)." (p. 39)
- "Inhalation serves as the expected primary route of exposure for the general population due to both its high volatility and propensity to be released to air from ongoing commercial and industrial activities." (p. 39)

With regards to water, EPA provides the following evidence that DCM contamination may be widespread in water:

- "Data compiled between 1992 and 2001 from NAWQA showed methylene chloride to be found in 6% of all ground water and surface water samples, with occurrences more common in surface water (U.S. EPA, 2009)." (p. 36)
- "Methylene chloride was detected in 20% of sediment samples in the STORET database (ATSDR, 2000)." (p. 36)
- "If methylene chloride-contaminated biosolids are released to the environment, including when the biosolids are land applied, methylene chloride will be present mainly in aqueous compartments based on its physical-chemical properties." (p. 53)
- "The general population may ingest methylene chloride via contaminated drinking water, ground water, and/or surface water. Ingestion of contaminated drinking water is expected to be the primary route of oral exposure." (p. 40)

However, EPA excludes such exposures in its Analysis Plan. The agency's rationale – "EPA has determined that the existing regulatory programs and associated analytical processes adequately assess and effectively manage the risks of methylene chloride that may be present in various media pathways (e.g., air, water, land) for the general population" (pp. 65-66) – is in direct contradiction with the explicit statements cited above that the agency expects the general population to be exposed to DCM via air and water.

Further, TSCA requires EPA to give particular attention to "potentially exposed or susceptible subpopulations" when assessing a chemical's risk. These are groups of people that are at greater risk of harm from a chemical due to biological reasons (e.g., children may be more vulnerable) or due to higher exposure (e.g., workers that directly handle the chemical). In the DCM Problem Formulation, EPA appropriately recognizes that people living or working near industrial sites manufacturing, processing, using, or disposing DCM are a "potentially exposed or susceptible subpopulation."

EPA specifically states:

> EPA identifies the following as potentially exposed or susceptible subpopulations that EPA expects to consider in the risk evaluation due to their *greater exposure*:
>
> ***
>
> - Other groups of individuals within the general population who may experience greater exposures due to their proximity to conditions of use identified in Section 2.2 that result in releases to the environment and subsequent exposures (e.g., individuals who live or work near manufacturing, processing, use or disposal sites). (p. 40)

The agency goes on to state:

> In summary, in the risk evaluation for methylene chloride, *EPA expects to analyze the following potentially exposed groups of human receptors*: workers, occupational non-users, consumers, bystanders associated with consumer use, and *other groups of*

individuals within the general population who may experience greater exposure. (pp. 41, emphasis added)

Yet, it appears that EPA does *not* in fact intend to evaluate DCM exposure to "individuals within the general population who may experience greater exposure," as the agency plans to ignore all exposures through air, water, and land – the very ways in which these groups of people may be or are exposed to DCM.

EPA must analyze these exposure pathways in order to produce a risk evaluation that is logically coherent and consistent with the best available science and available information establishing that exposure occurs through these pathways.

ii) EPA excludes additional exposure pathways based on insufficient evidence or illogical rationales.

In addition to exclusions on the basis of statutory arguments, EPA has made a number of inappropriate decisions to not further analyze specific exposure pathways or receptors with little or no explanation.

<u>EPA excludes the oral exposure route</u>. For consumers, EPA acknowledges the potential for exposure via hand to mouth behaviors but waves it off by stating that "[t]his exposure pathway will be limited by a combination of dermal absorption and volatilization." (p. 39) The oral exposure pathway for workers is ignored altogether. The absence of any analysis renders these decisions arbitrary and capricious.

<u>EPA excludes exposure to consumers from disposal</u>. EPA's rationale, with no supporting data or analysis, is that the agency, "does not expect exposure to consumers from disposal of consumer products. It is anticipated that most products will be disposed of in original containers, particularly those products that are purchased as aerosol cans." (p. 51) However, EPA then goes on to state that "liquid products may be recaptured in an alternate container following use (e.g. paint scrapings after paint removal as was done in EPA's 2014 risk assessment for methylene chloride paint stripping use)" (p. 51), providing a plausible mechanism by which consumers may be exposed during disposal.

<u>EPA excludes non-occluded dermal exposure to workers with little explanation</u>. In contrast, EPA does intend to consider non-occluded scenarios for consumers. EPA states:

> There is the potential for dermal exposures to methylene chloride in many worker scenarios. Where workers may be exposed to methylene chloride, the OSHA standard requires that workers are protected from contact (e.g. gloves) (29 CFR 1910.1052). EPA's 2014 risk assessment of methylene chloride paint stripping use included the potential dermal exposures to methylene chloride as an area of uncertainty that may underestimate the total exposures (U.S. EPA, 2014b). These dermal exposures would be concurrent with inhalation exposures and the overall contribution of dermal exposure to the total exposure is expected to be small however there may be exceptions for

> occluded scenarios. Occupational non-users are not directly handling methylene chloride; therefore, skin contact with liquid methylene chloride is not expected for occupational non-users and EPA does not expect to further analyze this pathway in the risk evaluation. *EPA expects to further analyze dermal exposures for skin contact with liquids in occluded situations for workers.* (p. 47, emphasis added)
>
> Workers and occupational non-users can have skin contact with methylene chloride vapor concurrently with inhalation exposures. The parameters determining the absorption of methylene chloride vapor are based on the concentration of the vapor, the duration of exposure and absorption. The concentration of the vapor and the duration of exposure are the same for concurrent dermal and inhalation exposures. Therefore, the differences between dermal and inhalation exposures depend on the absorption. The dermal absorption can be estimated from the skin permeation coefficient (0.28 cm/hr for methylene chloride vapor (ATSDR, 2010, 2000)) and exposed skin surface area (on the order of 0.2 m2 (U.S. EPA, 2011a)). The absorption of inhaled vapors can be estimated from the volumetric inhalation rate (approximately 1.25 m3/hr for a person performing light activity (U.S. EPA, 2011a) adjusted by a retention factor such as 0.75. *Based on these parameters the absorption of methylene chloride vapor via skin will be orders of magnitude lower than via inhalation and will not be further analyzed.* (p. 48, emphasis added)

That a smaller relative percentage of exposure to DCM will occur from dermal versus inhalation exposure does not mean that the dermal exposure is irrelevant to evaluating DCM risks in occupational settings. The contribution to DCM exposure from dermal absorption could still be significant. EPA should consider combined exposures to DCM via all pathways across all potential sources of exposure.

Moreover, EPA has not sufficiently justified why EPA will include occluded dermal exposures to workers but not non-occluded dermal exposure. Ostensibly, both exposures scenarios could result in frequent or continuous dermal contact and absorption to DCM, even if occluded exposures would tend to be higher.

EPA's rationale for ignoring non-occluded scenarios appears to be the mere existence of OSHA standard 29 CFR 1910.1052. Yet, in contrast to EPA's assertion that this standard requires use of protective gloves, this standard only requires respiratory protection and never mentions gloves. Thus, EPA's rationale appears to be flatly incorrect. As more accurately described in Appendix A:

> In 1997, OSHA revised an existing occupational safety and health standards [*sic*] for methylene chloride, to include an 8-hour TWA PEL of 25 ppm TWA, exposure monitoring, control measures and respiratory protection (29 CFR 1910.1052 App. A). (p. 84)

In sum, EPA's conclusory assertions are insufficient to justify its decisions, and EPA must analyze these pathways and receptors further. When EPA declines to analyze a pathway further, EPA must have

developed and applied a sound, rational basis for assessing the exposure level, supported by scientific evidence. In addition, EPA cannot then effectively ignore the exposure. Rather, EPA still must consider how the exposure may combine with other sources of exposure, so EPA must actually assess the level of exposure from the pathway individually and then consider how it combines with other sources of exposure.

C. EPA has not identified all relevant potentially exposed or susceptible subpopulations.

At the end of its section on Human Health Hazards (section 2.4.2.3), EPA states:

> In developing the hazard assessment, EPA will evaluate available data *to ascertain whether* some human receptor groups may have greater susceptibility than the general population to the chemical's hazard(s). (p. 45, emphasis added)

This statement stands in contrast to the analogous subsection under Human Exposure (p. 40), where EPA identified specific subpopulations that "EPA expects to consider in the risk evaluation due to their greater exposure." TSCA requires that EPA identify "potentially exposed or susceptible subpopulations," 15 U.S.C. § 2605(b)(4)(D), including those that "due to *** greater *susceptibility* *** may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture." 15 U.S.C. § 2602(12).

Unlike in the exposure section, EPA has not identified any vulnerable populations based on greater susceptibility. This needs to be remedied.

EPA's 2014 DCM risk assessment includes a section on susceptible subpopulations (3.3.2.4), proposing the following as subpopulations that may be more susceptible: smokers who maintain significant constant levels of carboxyhemoglobin; persons with existing cardiovascular disease; people with specific genetic polymorphisms for both GST theta-1 and CYP2E1; and the fetus and infants. EPA provides no rationale for not including at least these subpopulations in the DCM Problem Formulation. Given the evidence before the agency, EPA should identify these groups as relevant potentially susceptible subpopulations.

Further, EPA has deleted without explanation the following paragraph from the earlier DCM Scope under the analogous section:

> The IRIS assessment for methylene chloride indicates that there is some evidence that certain populations may be more susceptible to exposure to methylene chloride and examined lifestage, gender-specific, genetic variation, preexisting health status, lifestyle factors and nutrition status factors (U.S. EPA, 2011). Genetic polymorphisms that impact the enzymes that metabolize methylene chloride may lead to differences in susceptibility of individuals to the effects of methylene chloride and this susceptibility

> was quantified by (U.S. EPA, 2011). There are inadequate chemical-specific data to quantify the degree of differential susceptibility due to other susceptibility factors.[167]

It appears that EPA is going out of its way to avoid consideration of these susceptible subpopulations. They should be restored, along with any other relevant susceptible subpopulations.

41. EPA should rely on its prior hazard assessment in the current risk evaluation, and identify and justify any deviations from it.

EPA should rely heavily on the hazard characterization and dose response analysis done in the DCM risk assessment, which was conducted based on the best available science and has been peer reviewed.

Unfortunately, it appears that EPA plans only to use that assessment to identify relevant studies:

> Methylene chloride has an existing EPA IRIS Assessment (U.S. EPA, 2011b), an ATSDR Toxicological Profile (ATSDR, 2010, 2000), and assessments of the effects of acute exposures in the AEGL (NAC/AEGL, 2008), Spacecraft Maximum Allowable Concentrations (SMAC) for Methylene Chloride (NRC, 1996a) and an acute Recommended Exposure Limit (REL) published by the Office of Environmental Health Hazard Assessment (OEHHA) (OEHHA, 2008); hence, many of the hazards of methylene chloride have been previously compiled and reviewed. *EPA expects to use these previous analyses as a starting point for identifying key and supporting studies to inform the human health hazard assessment, including dose-response analysis.* The relevant studies will be evaluated using the data quality criteria in the *Application of Systematic Review in TSCA Risk Evaluations* document (U.S. EPA, 2018). EPA also expects to consider other studies (e.g., more recently published, alternative test data) that have been published since these reviews, as identified in the literature search conducted by the Agency for methylene chloride [*Methylene Chloride (CASRN 75-09-2) Bibliography: Supplemental File for the TSCA Scope Document* EPA-HQ-OPPT-2016-0742-0059 (U.S. EPA, 2017a)]. Based on reasonably available information, the following sections describe the potential hazards associated with methylene chloride. (pp. 44-45, emphasis added)

The agency indicates that "many of the hazards of methylene chloride have been previously compiled and reviewed," which was in fact done in the IRIS toxicological review (as well as the ATSDR profile). As described in the IRIS assessment, "[t]his document has been provided for review to EPA scientists, interagency reviewers from other federal agencies and White House offices, and the public, and peer reviewed by independent scientists external to EPA."[168] The IRIS assessment applied a systematic

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[167] U.S. EPA, *Scope of the Risk Evaluation for Methylene Chloride (Dichloromethane, DCM)* at 40 (June 2017), https://www.epa.gov/sites/production/files/2017-06/documents/mecl_scope_06-22-17.pdf.
[168] U.S. EPA, *Toxicological Review of Dichloromethane (Methylene Chloride) (CAS No. 75-09-2) In Support of Summary Information on the Integrated Risk Information System (IRIS)* at xxii (Nov. 2011), https://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/0070tr.pdf.

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review approach to the identification, consideration, and integration of the scientific literature bearing on the health effects of DCM. EPA relied heavily on the IRIS toxicological review to develop the DCM risk assessment.

In addition to the 2011 IRIS assessment, EPA relied on the AEGL, SMAC, and REL peer-reviewed reports for hazard and dose-response information. Further, the 2014 DCM risk assessment itself underwent a contractor-managed peer review that entailed three convenings of an expert panel during the fall of 2013, culminating in a peer review report.[169]

In describing the IRIS toxicological review and other assessments, EPA stated in the 2014 DCM risk assessment:

> EPA/OPPT used the DCM IRIS assessment as the principal data source for chronic toxicity hazard and dose-response information. The DCM IRIS assessment used a weight-of-evidence approach, the latest scientific information and physiologically-based pharmacokinetic (PBPK) modeling to develop hazard and dose-response assessments for carcinogenic and non-carcinogenic health effects resulting from lifetime exposure to DCM.
>
> The DCM IRIS assessment followed the principles set forth by the various risk assessment guidelines issued by the National Research Council (NRC) and EPA. Primary, peer-reviewed literature identified through September 2011 was systematically reviewed and included where that literature was determined to be critical to the assessment (EPA, 2011c).
>
> In addition, EPA/OPPT used the SMAC, the California acute REL and AEGL technical support documents as the data source for acute toxicity hazard and dose-response information. SMACs and the California acute REL for DCM are derived following the Guidelines for Developing Spacecraft Maximum Allowable Concentrations for Space Station Contaminants (NRC, 1992) and California's Air Toxics Hot Spots Program risk assessment guidelines for acute RELs (OEHHA, 1999), respectively. AEGLs are developed based on the criteria discussed in the Standing Operating Procedures (SOP) for Developing Acute Exposure Guideline Levels for Hazardous Chemicals (NRC, 2001).[170]

Given EPA's multiple, clear statements affirming the scientific rigor of the IRIS toxicological review, its use of other peer reviewed hazard assessments, as well as its decision to rely upon them in its 2014 DCM risk assessment and subsequent TSCA section 6 proposed ban, EPA should continue to rely on these earlier assessments. EPA must identify and explain any decision to deviate from these assessments and clearly identify in its draft risk evaluation any modifications it proposes in hazard

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[169] U.S. EPA Peer Review Panel, *OPPT Methylene Chloride (DCM) Draft Risk Assessment Final Comments of Nine-Member Peer Review Panel* (Dec. 31, 2013), https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/oppt-methylene-chloride-dcm-draft-risk-assessment-final.

[170] U.S. EPA, *TSCA Work Plan Chemical Risk Assessment Methylene Chloride: Paint Stripping Use* at 66-67 (Aug. 2014), https://www.epa.gov/sites/production/files/2015-09/documents/dcm_opptworkplanra_final.pdf.

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identification or dose-response characterization, and the scientific basis for them. Any such differences must be based on compelling scientific evidence and explicitly interrogated through the peer review process.

The excerpt from the DCM Problem Formulation cited above refers to "key," "supporting," and "relevant" studies. The meaning of these descriptors is entirely unclear. EPA must explicitly define the meaning of these terms and their implications with regard to the agency's approach to systematic review and risk evaluation.

EDF firmly believes that it is unnecessary – not to mention a waste of time and resources – to re-conduct aspects of the previous risk assessment unless EPA can demonstrate serious shortcomings of the previous assessments. EDF believes that the 2014 hazard assessment meets the best available science requirements and requires only minimal updating to reflect newer information. In particular, EPA has not provided any basis for redoing the dose-response analysis, as EPA suggests it may do on page 68. EPA should not redo the dose-response analysis, barring an exceptional and compelling basis for doing so.

42. EPA ignores important information gaps, and even where they are acknowledged, EPA provides no indication it intends to address them.

EPA has failed to use or signal any intent to use its TSCA section 4 and 8 information authorities, which were expanded under the 2016 TSCA amendments, to fill information gaps.

EPA's DCM Problem Formulation largely ignores information gaps altogether. For example, the 2014 DCM risk assessment identified both developmental neurotoxicity and immunotoxicity from chronic exposure as important information gaps:

> There is uncertainty about chronic exposure impacts on the nervous system function. The nervous system has been well studied and identified as very sensitive for acute effects. However, there is a paucity of data on chronic neurological impacts, especially developmental neurotoxicity. Likewise, there is limited information about immunotoxicity following chronic exposure to DCM. Existing hazard studies are not sufficient for dose response analysis to provide a lower point of departure than existing adverse findings in the liver from chronic exposures.[171]

Yet the problem formulation does not even mention these data gaps – let alone describe a strategy for acquiring the needed information.

[171] U.S. EPA, *TSCA Work Plan Chemical Risk Assessment Methylene Chloride: Paint Stripping Use* at 115 (Aug. 2014), https://www.epa.gov/sites/production/files/2015-09/documents/dcm_opptworkplanra_final.pdf.

While EPA expressly acknowledges few data gaps in the Problem Formulation, the existence of exposure information gaps is implied through EPA's plan to use surrogate data and models rather than using its information authorities to obtain exposure information on DCM.

With regards to surrogate data, EPA specifically proposes to:

- "Review reasonably available measured or estimated release data for surrogate chemicals that have similar uses and chemical and physical properties. Data for solvents that are used in the same types of applications may be considered as surrogate data for methylene chloride. As with methylene chloride, trichloroethylene is used in paints and coatings, in adhesives and sealants, and as solvents for cleaning and degreasing." (p. 60)

- "For several uses including use of adhesives, cleaners, and laundry and dishwashing products, EPA believes that trichloroethylene and other similar solvents may share the same or similar conditions of use and may be considered as surrogates for methylene chloride." (p.63)

While EDF does not oppose including surrogate data when relevant, it should not be the option of first resort or be used as an excuse to fail to actively obtain such data through use of EPA's information authorities.

Where EPA does acknowledge information gaps (see below), it fails to set forth a plan to use its TSCA section 4 and 8 information authorities to fill such gaps. For example:

- Breastmilk as an exposure route: "Methylene chloride and its metabolites have been measured in expired air, blood, urine and breast milk however methylene chloride measurements in human milk have not been quantified and there are no animal studies testing to what extent methylene chloride can pass into milk (ATSDR, 2000)." (p. 36)
    - Given the greater susceptibility of infants to DCM (as their hemoglobin has a higher affinity for carbon monoxide than adult hemoglobin[172]), breastmilk may be an important exposure pathway to consider. In this excerpt, EPA acknowledges that the necessary data do not exist, yet indicates no intent to promulgate a section 4 order or rule to develop such information.

- Acute sediment toxicity studies: "There were no available acute sediment toxicity studies, however, toxicity is expected to be similar to that of aquatic invertebrates when exposed to methylene chloride in sediment pore water." (p. 42)
    - EPA provides no justification for why sediment invertebrates are expected to have a similar toxicity profile as aquatic invertebrates. A sediment toxicity test is a simple

[172] U.S. EPA, *TSCA Work Plan Chemical Risk Assessment Methylene Chloride: Paint Stripping Use* at 82 (Aug. 2014), https://www.epa.gov/sites/production/files/2015-09/documents/dcm_opptworkplanra_final.pdf (referencing OEHHA 2001 at https://oehha.ca.gov/media/downloads/air/report/sb2520tac20prioritization.pdf).

protocol that EPA could easily mandate through a section 4 order or rule within the given timeframe.

- Occupational exposures: "For some OSHA data, NAICS codes included with the data will be matched with potentially applicable conditions of use, and data gaps will be identified where no data are found for particular conditions of use. EPA will attempt to address data gaps identified as described in steps 2 and 3 below." (p. 63)
    - Step 2 entails the use of data on surrogate chemicals and Step 3 entails the use of models. No step is indicated that would entail requiring submission or development of the needed data.

EPA should use its information authorities to fill all of these information gaps.

43. The DCM Problem Formulation utilizes assumptions and models that are unclear or not necessarily conservative.

Despite its assertions, EPA uses or suggests it will use non-conservative assumptions at various points in the DCM Problem Formulation. Two examples are provided below.

A. Exposures to terrestrial species.

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

EPA initially states, "Terrestrial species populations living near industrial and commercial facilities using methylene chloride may be exposed via multiple routes such as ingestion of surface waters and inhalation of outdoor air." (p. 37)

However, EPA will not further analyze exposure to terrestrial organisms through water, sediment, or migration from biosolids via soil deposition, based on the assertion that "[t]errestrial species exposures to MC in water are orders of magnitude below hazardous concentrations." (Appendix E, pp. 139-140)[173]

Yet EPA has not shown any analysis or calculations and has not provided any citations to data sources to support this statement; it is simply asserted.

Furthermore, EPA has not bothered to calculate acute and chronic concentrations of concern (COC) as it has done in its other problem formulations. EPA explicitly states that it has not applied adjustment factors to the hazard levels listed on pp. 43-44:

> It should be noted that these hazard levels of concern do not account for differences in inter- and intra-species variability, as well as laboratory-to-field variability and are

[173] EPA also excludes exposure to terrestrial organisms from the ambient air pathway based on the inappropriate argument that such exposures are adequately managed by the Clean Air Act (see Section 5.C).

> dependent upon the availability of datasets that can be used to characterize relative sensitivities across multiple species within a given taxa or species group, since the data available for most industrial chemicals are limited. (p. 44)

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

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

It is far from clear from the DCM Problem Formulation how EPA managed to conclude that DCM in water is orders of magnitude below concentrations of concern, but it appears the agency did not take a conservative approach in arriving at this conclusion. EPA needs to provide a rational and clear analysis based on the best available science and reasonably available information to support its conclusions, and at this point, it has failed to do so.

B. Occupational exposure via inhalation route.

Under its Analysis Plan, EPA implies that it may rely on U.S. Occupational Safety and Health Administration's (OSHA) Permissible Exposure Limit (PEL):

> This or other models, including the *assumption of compliance with the OSHA PEL* for methylene chloride, may be explored where models specific to conditions of use are not found. (p. 63, emphasis added)

In general, it makes no sense to default to a standard unless there is strong empirical evidence that workplaces universally comply with the standard. In the case of DCM specifically, there is significant evidence from workplace monitoring studies that levels exceed the current OSHA PEL for DCM of 25 ppm (8-hour time-weighted average).

For example, EPA's proposed section 6 rule to ban DCM in paint and coating removal products explains:

> It is important to note that EPA relied on monitoring data for these occupational exposure estimates. 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).[174]

Even these levels may have been an underestimate of DCM exposure. Comments submitted by a former OSHA official to the docket on EPA's proposed section 6 rule on DCM argued that the agency underestimated exposure levels. The commenter provided an OSHA dataset including 12,152 personal air samples OSHA collected on DCM between 1984 and 2016. He summarized the results as follows:

> The data I've provided show that the AVERAGE MeCl2 concentration from 1984 to April 1999 (at which point our 1997 standard took full effect) was about 85 ppm, but the average since then has only dropped to 72 ppm![175]

It makes no sense for EPA to rely on the PEL as a default given the existence of real-world monitoring data demonstrating that it is regularly exceeded.

It also bears mentioning that OSHA's PEL of 25 ppm is itself not health-protective. It was last updated in 1997 – over 20 years ago – and EPA's proposed section 6 rule on DCM and NMP concluded that OSHA's PEL is higher than the levels at which EPA identified unreasonable risk.[176] Furthermore, OSHA itself has indicated[177] that the PEL would be insufficient to protect workers from the risks identified by EPA in the context of paint and coating removal exposures.

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

44. EPA's problem formulation contains several statements relating to confidential business information (CBI) that are or may be inconsistent with its authorities and obligations under TSCA.

EPA states: "EPA may consider any relevant confidential business information (CBI) in the risk evaluation in a manner that protects the confidentiality of the information from public disclosure." (p. 59)

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[174] Methylene Chloride and N-Methylpyrrolidone; Regulation of Certain Uses Under TSCA Section 6(a), 82 Fed. Reg. 7464, 7477 (proposed Jan. 19, 2017), https://www.regulations.gov/docket?D=EPA-HQ-OPPT-2016-0231.

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

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

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

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This statement ignores the major changes made to the CBI provisions of TSCA section 14. Companies must substantiate most claims for CBI protection and EPA must review many of them within 90 days of submission of the information. Any claim that does not meet all applicable requirements cannot be protected from disclosure.

Further, EPA fails to acknowledge that health and safety studies are expressly not eligible for protection as CBI under TSCA, subject only to two very narrow exceptions. *See* 15 U.S.C. § 2613(b)(2). All such information not subject to the exceptions needs to be made public.

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Comments on NMP

45. EPA needs to finalize its proposed ban of NMP in paint and coating removal products and not use the larger ongoing risk evaluation of NMP as a reason for delay.

EDF incorporates by reference its comments on EPA's proposed rule to restrict NMP in paint and coating removal products.[178] EPA's 2015 NMP Work Plan risk assessment (hereafter "NMP risk assessment") and supplemental technical reports make clear that NMP, under the conditions of use subject to the proposed rule, presents an unreasonable risk of adverse developmental outcomes to women of childbearing age from both acute (fetal mortality) and chronic (decreased fetal body weight) NMP exposure. These evaluations reflect the input from numerous and extensive peer reviews, incorporate the best available science, and apply a weight-of-the-scientific-evidence approach.

The Lautenberg Act clearly intended for EPA to move forward to address risks it identified in assessments completed prior to enactment.

Section 26(l)(4) states (emphases added):

> (4) CHEMICAL SUBSTANCES WITH COMPLETED RISK ASSESSMENTS.—With respect to a chemical substance listed in the 2014 update to the TSCA Work Plan for Chemical Assessments for which the Administrator has *published a completed risk assessment prior to the date of enactment* of the Frank R. Lautenberg Chemical Safety for the 21st Century Act, the Administrator *may publish proposed and final rules under section 6(a)* that are consistent with the scope of the completed risk assessment for the chemical substance and consistent with other applicable requirements of section 6.

Section 26(p)(3) states (emphasis added):

> (3) ACTIONS COMPLETED PRIOR TO COMPLETION OF POLICIES, PROCEDURES, AND GUIDANCE. – *Nothing in this Act requires the Administrator to revise or withdraw a completed risk evaluation, determination, or rule* under this Act solely because the action was completed prior to the development of a policy, procedure, or guidance pursuant to the amendments made by the Frank R. Lautenberg Chemical Safety for the 21st Century Act.

These provisions of the law make abundantly clear that EPA can proceed to promulgate a rule based on its completed NMP risk assessment and is under no obligation to withdraw its prior risk assessment, risk determination or proposed rule. Indeed, Congress included these provisions for the very purpose of grandfathering-in the Work Plan risk assessments EPA had completed and ensuring its authority to use those assessments as the basis for section 6 risk management rules.

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[178] EDF Comments on Regulation of Certain Uses under Toxic Substances Control Act: Methylene Chloride and N-Methylpyrrolidone, https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0231-0912.

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Furthermore, the very high risks EPA has identified for the conditions of use subject to the proposed rule demand that the agency move expeditiously to finalize the rule. It is indefensible for EPA to delay critically needed action on paint stripping products by, as EPA now plans to do, reevaluating those conditions of use in the current risk evaluation. This approach will effectively delay action for years – putting workers', consumers' and the public's health at risk.

EPA needs to expeditiously finalize option 1 of its proposed section 6(a) rule to ban NMP's use in paint stripping products.[179] Then, in the current risk evaluation, it also must take into consideration any exposures remaining from those uses despite that rule due, for example, to any allowed exemptions.

46. EPA should rely on its prior hazard assessment in the current risk evaluation, and identify and justify any deviations from it.

EPA should rely heavily on the hazard characterization and dose response analysis done in the NMP risk assessment, which was conducted based on the best available science and has been peer reviewed.

Unfortunately, it appears that EPA plans only to use that assessment to identify relevant studies:

> EPA expects to evaluate all potential hazards for NMP, using the previous analysis as a starting point for identifying key and supporting studies and including any information found in recent literature. The relevant studies will be evaluated using the data quality criteria provided in the *Application of Systematic Review in TSCA Risk Evaluations* document (U.S. EPA, 2018). (p. 10)

U.S. EPA, Problem Formulation of the Risk Evaluation for N-Methylpyrrolidone (2-Pyrrolidinone, 1-Methyl-) at p. 10 (May 2018), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0743-0076. Is EPA planning to use its prior assessment *only* for the purpose of identifying "key" studies? If so, on what basis is it rejecting the hazard assessment? If EPA now believes there are flaws or shortcomings in the earlier assessment, it should clearly identify them and provide the basis for its beliefs.

EPA's NMP risk assessment involved a critical consideration of the scientific literature that, among other evidence, included a number of authoritative, peer-reviewed reports such as:

- The Dutch National Institute for Public Health and the Environment (RIVM) Proposal for a Restriction of NMP[180]

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

[180] RIVM (National Institute for Public Health and the Environment (RIVM)), *Annex XV Restriction Report: Proposal for a Restriction, N-Methylpyrrolidone (NMP)* (2013), https://echa.europa.eu/documents/10162/2a5f3a2e-6f9c-08ac-6e44-4e4792b5cba9.

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- Organization for Economic Co-operation and Development (OECD) SIDS Initial Assessment Report[181]

- WHO Concise International Chemical Assessment Document (CICAD) for NMP[182]

- Cal OEHHA Maximum Allowable Dose Levels (MADL) for NMP[183]

The NMP risk assessment itself was peer-reviewed through a contractor-managed peer review process, culminating in a peer review report.[184] In addition, opportunities for public comment were provided upon issuance of the draft risk assessment (Jan – March 2013)[185] and in conjunction with each of the three expert panel meetings.[186]

EDF firmly believes that it is unnecessary – not to mention a waste of time and resources – to re-conduct aspects of the previous risk assessment unless EPA can demonstrate serious shortcomings in the previous assessment. EDF believes that the 2015 hazard assessment meets the best available science requirements and requires only minimal updating to reflect newer information and consideration of susceptible subpopulations (see Section 47.B.i below). In particular, EPA has not provided any basis for redoing the dose-response analysis, as the agency suggests it may do on page 60. EPA should not redo the dose-response analysis, barring an exceptional and compelling basis for doing so.

47. EPA has excluded or failed to sufficiently identify and analyze relevant exposure pathways and vulnerable subpopulations for NMP.

A. Exposure pathways are inappropriately excluded.

EPA's NMP Problem Formulation – Problem Formulation of the Risk Evaluation for N-Methylpyrrolidone (2-Pyrrolidinone, 1-Methyl-) (May 2018), https://www.regulations.gov/document?D=EPA-HQ-OPPT-

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[181] Organization for Economic Co-operation and Development, *SIDS Initial Assessment Report. 1-Methyl-2-Pyrrolidone* (2007), https://hpvchemicals.oecd.org/UI/handler.axd?id=84daa4ac-feb7-4b5a-9839-206d17914e42.

[182] World Health Organization, *Concise International Chemical Assessment Document (CICAD) 35, N-Methyl-2-Pyrrolidone* (2001), www.who.int/entity/ipcs/publications/cicad/en/cicad35.pdf.

[183] Office of Environmental Health Hazard Assessment, *Proposition 65 Maximum Allowable Dose Level (MADL) for Reproductive Toxicity for N-Methypyrrolidone for Dermal and Inhalation Exposures. Reproductive and Cancer Hazard Assessment Section* (2003), https://oehha.ca.gov/media/downloads/proposition-65/chemicals/nmpmadl31403.pdf.

[184] U.S. EPA Peer Review Panel, *OPPT N-Methylpyrrolidone (NMP) Draft Risk Assessment Final Comments of Nine Member Peer Review Panel* (Dec. 2013), https://www.epa.gov/sites/production/files/2015-09/documents/nmp_consolidated_peer_review_comments_december_31_2013.pdf.

[185] Public comment opportunities were available at docket number EPA-HQ-OPPT-2012-0725. *See* https://www.regulations.gov/document?D=EPA-HQ-OPPT-2012-0725-0001.

[186] *Dichloromethane and NMethylpyrrolidone TSCA Chemical Risk Assessment; Notice of Public Meetings and Opportunity to Comment*, 78 Fed Reg. 52525 (Aug. 23, 2013), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2012-0725-0036.

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2016-0743-0076 (hereafter "NMP Problem Formulation") – is largely irrational and often incoherent, with the agency both: 1) acknowledging many exposures that it later excludes, and 2) choosing to ignore exposure pathways with little or no explanation.

i) Major deficiencies and inconsistencies abound in EPA's assertion that exposures to NMP falling under other legal jurisdictions are adequately managed.

EPA has chosen to exclude all exposures to the general population based on the rationale that other statutes cover such exposures to air, water, and land contamination. We have explained elsewhere why this is an illegal and unsound approach (see Section 5). It is also illogical, as the NMP Problem Formulation itself points to potential risks to the general population from such exposures.

For example, EPA acknowledges that:

- "NMP has been detected in industrial landfill leachate;" (p. 33)
- "NMP has been detected in wastewater;" (p. 36)
- "Oral exposure to NMP is expected to be a relevant route of exposure for the general population." (p. 36)

However, such exposures are ultimately excluded in EPA's Analysis Plan. EPA's rationale for excluding oral exposure via drinking water to the general population is the mere existence of the Safe Drinking Water Act. There is no National Primary Drinking Water regulation for NMP; it is only listed on the EPA's fourth Contaminant Candidate List (CCL), which EPA itself describes as a "list of unregulated contaminants." In fact, being placed on the CCL is just the first of a long series of steps that must be taken before it is considered for regulation:

> Once contaminants have been placed on the CCL, EPA identifies if there are any additional data needs, including gaps in occurrence data for evaluation under Regulatory Determination; if sufficient occurrence data is lacking, the contaminant may be considered for monitoring under the Unregulated Contaminant Monitoring Rule. (p. 49)

Such monitoring is required to be considered for regulation:

> EPA must publish a CCL and make Regulatory Determinations to regulate at least five CCL contaminants every 5 years. To regulate a contaminant, EPA must conclude the contaminant may have adverse health effects, *occurs or is substantially likely to occur in public water systems at a level of concern* and that regulation, in the sole judgement of the Administrator, presents a meaningful opportunity for health risk reduction. (p. 49, emphasis added)

Yet EPA argues that this long and uncertain process is a sufficient basis to ignore drinking water exposures to the general population, because "NMP is being addressed under the regular analytical processes used to identify and evaluate drinking water contaminants of potential regulatory concern for

public water systems under SDWA." (p. 49) This statement stands in direct contrast with EPA's statement earlier in the NMP Problem Formulation document acknowledging there are ongoing exposures to the general population from drinking water. Given empirical evidence establishing these ongoing exposures, EPA must analyze exposures to NMP through the drinking water pathway. EPA must analyze exposures through the other pathways as well, for reasons articulated above.

ii) EPA will not further analyze additional exposure pathways based on insufficient evidence or illogical rationales.

EPA has made a number of decisions not to further analyze specific exposure pathways or receptors with little or no explanation.

1) EPA excludes oral exposure for workers with no explanation. Oral exposure is not included as an exposure route for industrial and commercial activities in EPA's conceptual model. (p. 44) While EPA does note that "[I]ncidental ingestion of inhaled NMP (vapor/mist/dust) will be considered as inhalation exposure," (pp. 42, 44) it is unclear why EPA is not evaluating ingestion of NMP from hand-to-mouth or other direct ingestion pathways. EPA's failure to provide a reasoned basis for excluding this exposure pathway is arbitrary and capricious. Notably, EPA does intend to evaluate this exposure route for consumers. (pp. 45, 46)

2) EPA has decided not to further analyze risk to sediment invertebrates or terrestrial organisms (the latter of which EPA notes include soil-dwelling organisms) based on insufficient evidence. EPA has not identified any data on hazards to sediment invertebrates or terrestrial organisms, yet has decided not to further analyze the risk to these organisms because "exposure to soil- or sediment-dwelling organisms is not expected to be significant" – a statement that excludes many types of terrestrial organisms. (p. 38) With respect to soil- or sediment-dwelling organisms, EPA asserts this claim based on the physical-chemical and fate properties of NMP – not any actual exposure monitoring data or even modeling. EPA cites Section 2.3.4 of the problem formulation as providing support for its decision not to further analyze exposure to soil- or sediment-dwelling organisms. (p. 38) Yet Section 2.3.4: 1) does not apply to sediment-dwelling organisms at all, and 2) to the extent that the terrestrial population subsection of section 2.3.4 applies to soil-dwelling organisms, it indicates that they in fact may be exposed to NMP "via multiple routes." (p. 34) If anything, this section suggests that exposure to terrestrial organisms warrants further analysis.

Elsewhere, EPA makes another unsupported assertion for why it will not further analyze the sediment pathway: "NMP toxicity to sediment-dwelling invertebrates is expected to be comparable to that of aquatic invertebrates." (p. 47). But EPA never provides data or analysis to support this expectation, and EPA never explains why it will not further analyze exposures to soil-dwelling organisms. In the end, EPA provides no rationale for declining to analyze risk to terrestrial organisms.

Importantly, exposures cannot be characterized as low absent hazard information. It is certainly possible that NMP is sufficiently toxic to organisms that even "low" levels of exposure pose

> significant risk. EPA must use its information authorities to obtain more information about risks to sediment-dwelling organisms and terrestrial organisms, and EPA must actually evaluate the risks presented to these organisms.
>
> 3) EPA plans not to further analyze exposures to humans from releases to ambient surface water on the basis that a first-tier analysis resulted in a calculated margin of exposure (MOE) for oral, inhalation, and dermal exposure of 338, which exceeded EPA's proposed benchmark MOE of 30, "indicating a low risk concern." (p. 47) But this analysis examines this one pathway in isolation from all others. If EPA were to combine this exposure with those from other pathways resulting from this and other conditions of use the contribution from ambient surface water may very well be significant.

EPA must analyze these pathways and receptors further, or provide a scientifically and logically sound basis for their exclusion, reflecting the best available science and reasonably available information about these exposures and receptors. Where EPA has inadequate information, EPA must use its information authorities to obtain additional information. EPA also must consider how exposures through these pathways combine with other exposures to present an unreasonable risk; EPA cannot simply consider them in isolation and then dismiss them on that basis.

B. Vulnerable subpopulations.

i) Vulnerable subpopulations are inappropriately excluded.

TSCA requires EPA to give particular attention to "potentially exposed or susceptible subpopulations" when assessing a chemical's risks. These are groups of people that are at greater risk of harm from a chemical due to biological reasons (e.g., children who may be more vulnerable) or due to higher exposure (e.g., workers that directly handle the chemical). In the NMP Problem Formulation, EPA appropriately recognizes that people living or working near sites manufacturing, processing, using, or disposing NMP are a "potentially exposed or susceptible subpopulation."

EPA specifically states:

> EPA identifies the following as potentially exposed or susceptible subpopulations that EPA expects to consider in the risk evaluation due to their *greater exposure*:
>
> ***
>
> - Other groups of individuals within the general population who may experience greater exposures due to their proximity to conditions of use identified in Section 2.2 that result in releases to the environment and subsequent exposures (e.g., individuals who live or work near manufacturing, processing, use or disposal sites). (p. 37)

The agency goes on to state:

> In summary, in the risk evaluation for NMP, EPA expects to analyze the following potentially exposed groups of human receptors: workers, occupational non-users, consumers, bystanders associated with consumer use and *other groups of individuals within the general population who may experience greater exposure* (pp. 38-39, emphasis added)

Yet, it appears that EPA does *not* in fact intend to evaluate NMP exposure to "individuals within the general population who may experience greater exposure," as the agency plans to ignore all exposures through air, water, and land – the very ways in which this subpopulation may be exposed to NMP.

EPA's NMP Conceptual Model for Environmental Releases and Wastes (Figure 2-4, p. 52) includes a footnote in the "Receptors" section that states: "Receptors include potentially exposed or susceptible subpopulations." However, every single receptor is greyed out in this conceptual model (indicating that the agency does not intend to further analyze these pathways) – including the general population, and by implication, those subpopulations within the general population living near manufacturing, processing, use or disposal sites. Thus, EPA's conceptual model indicates that EPA intends to ignore the very subpopulations that EPA elsewhere identified as relevant and meriting analysis. EPA's incoherent approach to these subpopulations and exposures is arbitrary and capricious.

It is worth noting that as part of its justification for ignoring the ambient air pathway, EPA cites an analysis from the 2015 NMP risk assessment that predated the 2016 TSCA reforms and hence did not take into consideration the agency's new mandate to identify and evaluate risks to "potentially exposed or susceptible subpopulations." In that earlier assessment, EPA used default exposure factors that are non-specific, and were not appropriate to the susceptible subpopulation of women of childbearing age and children (see Section 47.B.ii below). For example, EPA used an 80-kg body weight (p. 48), while EPA's 2017 Exposure Factors Handbook[187] indicates that the mean weight for women between 16 and <40 years of age ranges from 65.9 – 74.8 kg. If EPA had used a lower body weight in its calculations, it would have derived a lower point of departure (POD). Children have an even lower body weight: for example, infants from birth to <1 month weigh 4.8 kg; toddlers 1 to <2 years old weigh 11.4 kg; and children 6 to <11 years weigh 31.8 kg.

It appears EPA's "first-tier" analysis, which it uses as the basis to exclude ambient air exposures for "Adults and children living near facilities" (p. 126), ignored the most susceptible subpopulations. Moving forward, EPA must take into consideration exposure factors relevant to potentially exposure or susceptible subpopulations, given the new statutory requirement.

ii) EPA has not identified all relevant potentially exposed or susceptible subpopulations.

At the end of its section on Human Health Hazards (section 2.4.2.3), EPA states:

> In developing the hazard assessment, *EPA will analyze available data to ascertain whether some human receptor groups may have greater susceptibility than the general*

[187] U.S. EPA, Exposure Factors Handbook: 2011 Edition at 8-14 (Sept. 2011), https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=236252.

population to the chemical's hazard(s). In the previous risk assessment (U.S. EPA, 2015), EPA identified young children and pregnant women as potentially susceptible subpopulations. (p. 41, emphasis added)

In setting the scope of a problem formulation, TSCA requires that EPA identify "potentially exposed or susceptible subpopulations," 15 U.S.C. § 2605(b)(4)(D), including those that "due to *** greater *susceptibility* *** may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture." 15 U.S.C. § 2602(12) (emphasis added).

While EPA acknowledges that its 2015 NMP risk assessment identified concerns specific to young children and pregnant women, EPA has failed to identify such subpopulations as ones that EPA expects to consider due to greater susceptibility in its forthcoming evaluation. Given the evidence EPA cites for reproductive and developmental toxicity, these subpopulations at a minimum need to be identified as potentially exposed or susceptible subpopulations.

This omission of specific subpopulations stands in contrast to the analogous subsection under Human Exposure (p. 37), where EPA identified specific subpopulations that "EPA expects to consider in the risk evaluation due to their greater exposure." This needs to be remedied.

48. EPA ignores important information gaps, and even where others are acknowledged, EPA provides no indication it intends to address them.

EPA has failed to use or signal any intent to use its TSCA section 4 and 8 information authorities, which were expanded under the 2016 TSCA amendments, to fill information gaps.

For example, the 2015 NMP risk assessment identifies a number of important data gaps for both hazard (e.g., neurotoxicity) and exposure (e.g., glove effectiveness for dermal exposure, air monitoring data for inhalation exposure). Pages 95-101 of the 2015 NMP risk assessment[188] detail these data gaps, which are further acknowledged in the NMP proposed section 6 rule.[189] Yet not only has EPA made no attempt to fill these key data gaps, it has not even acknowledged them in the NMP Problem Formulation. EPA should use its information authorities to fill these gaps.

For other data gaps that EPA does acknowledge in the NMP Problem Formulation (e.g., "EPA did not identify water monitoring data for NMP during its review of the national surface water monitoring database," (p. 33), EPA does not describe any strategy for acquiring such data. Instead, EPA indicates it will rely on measured or estimated release data for surrogate chemicals for NMP as well as models (p. 54). While EDF does not oppose including surrogate data when relevant, it should not be the option of

[188] U.S. EPA, TSCA Work Plan Chemical Risk Assessment N-Methylpyrrolidone: Paint Stripper Use CASRN: 872-50-4 at 95-101 (Mar. 2015), https://www.epa.gov/sites/production/files/2015-11/documents/nmp_ra_3_23_15_final.pdf.

[189] Methylene Chloride and N-Methylpyrrolidone; Regulation of Certain Uses Under TSCA Section 6(a), 82 Fed. Reg. 7464, 7519 (proposed Jan. 19, 2017), https://www.regulations.gov/docket?D=EPA-HQ-OPPT-2016-0231.

first resort or be used as an excuse to fail to actively pursue such data through its information authorities.

EPA appears adamant on resorting to models and surrogate data even though it has clear authority to require the development of information to fill gaps or resolve discrepancies and uncertainties in the available data. For example, under its Analysis Plan for occupational exposures, EPA states: "Data gaps will be identified where no data are found for specific conditions of use. EPA will attempt to address data gaps identified as described in steps 2 and 3 below." (p. 56) Step 2 entails the use of data on surrogate chemicals and Step 3 entails the use of models. No step is indicated that would entail requiring submission or development of the needed data.

As a result, EPA's decisions in its risk evaluation and any subsequent risk management will be accompanied by unnecessary large degrees of uncertainty. Instead, EPA should rely on its information authorities to obtain additional information.

As described above, EPA has not identified any data on hazards to sediment invertebrates or terrestrial organisms. Here, EPA does not even bother with surrogate data, but claims that "NMP toxicity to sediment-dwelling invertebrates is expected to be comparable to that of aquatic invertebrates." (p. 47) EPA makes this assertion with absolutely no justification. EPA can and should mandate section 4 order or test rules to acquire data on the toxicity of NMP to sediment invertebrates and terrestrial organisms.

Similarly, as described more below, EPA appears to have relatively little information on hazards for aquatic organisms, particularly on chronic hazards, which limits its ability to identify a chronic concentration of concern (COC). EPA should similarly mandate chronic toxicity testing on aquatic organisms.

49. The NMP Problem Formulation demonstrates a lack of conservatism in assumptions and models.

Despite its assertions, EPA uses or suggests it will use non-conservative assumptions throughout the NMP Problem Formulation. Two examples are provided below.

A. Surface water pathway and risk to aquatic species

EPA asserts that its COCs for aquatic effects and its modeled surface water concentrations are "conservative." These statements are inaccurate.

With regards to the acute COC, EPA states:

> The acute COC of 246 µg/L, derived from the experimental aquatic invertebrate endpoint, is used as a *conservative* hazard level for NMP in this problem formulation. (p. 40, emphasis added)

With regards to the chronic COC, EPA states:

> The chronic COC of 1,768 µg/L, derived from the experimental aquatic invertebrate endpoint, is used as the *lower bound* hazard level for NMP in this problem formulation. (p. 40, emphasis added)

First, EPA implies that its calculations of COCs are conservative at least in part because of its use of assessments factors. The use of such factors is not conservative: They account for *real-world sources of variability as well as database limitations*, and cannot be construed as "safety factors" that yield conservative estimates.[190] As EPA states:

> The application of assessment factors is based on established EPA/OPPT methods (U.S. EPA, 2013, 2012d) and were used in this hazard assessment to calculate lower bound effect levels (referred to as the concentration of concern; COC) that would likely encompass more sensitive species not specifically represented by the available experimental data. Also, assessment factors are included in the COC calculation to account for differences in inter- and intraspecies variability, as well as laboratory-to-field variability. (p. 39)

We identify further concerns with these COCs below.

Second, EPA's modeling exercise to identify potential exposure to aquatic species is not as conservative as it suggests. EPA states:

> EPA employed a first-tier screening approach, utilizing readily-available data, modeling tools and conservative assumptions. EPA's Probabilistic Dilution Model (PDM) was used to estimate site-specific surface water concentrations based on the 2015 TRI data for "on-site" NMP releases to surface waters (U.S. EPA, 2007). The reported TRI releases were based on available information including monitoring data, emission factors, mass balance and/or other engineering calculations. The PDM also incorporates wastewater treatment removal efficiency. For this analysis, wastewater treatment removal efficiency was conservatively assumed to be 0%, as the reported NMP water releases were assumed to account for wastewater treatment *a priori*. Further, as the total days of release were not reported in these sources, EPA assumed a range of possible release days (i.e., 12 and 250 days/year) for facilities directly discharging NMP to surface water and 250 days/year for indirect discharges from wastewater treatment plants or Publicly Owned Treatment Works (POTWs) receiving indirect discharges of NMP).
>
> The "high-end" surface water concentrations (i.e., those obtained assuming a low stream flow for the receiving water body) from all PDM runs ranged from 224 µg/L to 0.00005 µg/L, for the acute (i.e., assumed fewer than 20 days of environmental releases per year) and chronic exposure scenario (i.e., more than 20 days of environmental releases per year assumed), respectively. (pp. 33-34)

Yet the modeling makes assumptions that are not conservative:

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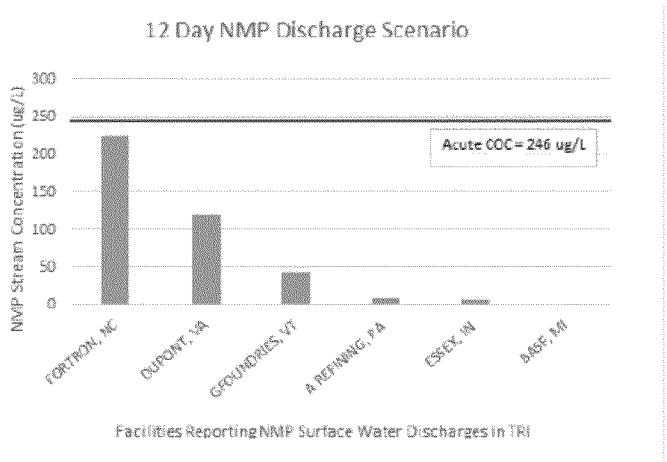
[190] *See* above at Section 14.

- *Days of release*: EPA provides no explanation of how it selected the numbers of release days (12 and 250) per year it used, nor why it selected yet another value – 20 days[191] – as the line between acute and chronic exposures. Given that EPA is using a fixed TRI release value, the best assumption for acute exposure (which might well not be at all conservative) would be to assume the release occurs in a single day. Compared to the 12 or 20 release-day scenarios utilized, this would result in considerably higher acute exposure estimates. Barring any actual data, this would be most appropriate assumption.

- *Sources of exposure*: In modeling surface water concentrations, EPA only considers the 14,092 lb/year of NMP directly and indirectly released to surface water, based on 2015 TRI data. This does not account for the estimated 6,438,594 million pounds released into land based on 2015 TRI data. Elsewhere EPA asserts that, due to its physical chemical properties, NMP will readily partition out of soil into water (e.g., "NMP exhibits high mobility in soil; hence, environmental releases are expected to migrate from soil to ground water," p. 30). How has EPA ruled out that any of the large quantities of NMP released to land do not end up in surface water? The only attempt at a rationale is the speculative statement that "[m]igration of NMP between ground water and surface water has not been documented, but may be mitigated by abiotic and biotic degradation in the water column." (p. 48)

Third, while not as conservative as EPA asserted, its modeling exercise still estimated high-end surface water concentrations at 224 µg/L, based on a facility located in Wilmington, NC (see Table_Apx C-1, p. 91). This value is so close to the acute COC of 246 µg/L that it should compel further data development and analysis beyond EPA's cursory first-tier analysis. *See* Figure Apx C-1 below.

Figure Apx C-1. Estimated Surface Water Concentration for 12-Day NMP Discharge



Fourth, it makes little sense for a chronic COC to be higher than the acute COC (specifically, over 7x higher). Logically, a concentration that causes acute effects should cause at least that same effect when

[191] EPA's invoking of 20 days is curious, as that value appears nowhere else in the document.

a species is subjected to it over a longer period of time. Bizarrely, this disparity in the data is present despite the fact that the chronic and acute values were both derived from testing on water fleas.

In the absence of reliable chronic data (a data gap EPA should use its information authorities to fill), a more conservative estimate would use the lowest acute value (1.23 mg/L) and divide it by an appropriate acute-to-chronic ratio (ACR) – as EPA did in its 1-BP problem formulation – as well as the assessment factor of 10 that EPA used to derive the chronic COC. EPA used an ACR of 10 in its 1-bromopropane Problem Formulation (p. 43); however, a cursory search of the literature indicates that an ACR of at least 100 may be needed to be sufficiently protective for most chemicals.[192] Applying an ACR of 100 and the assessment factor of 10, a more appropriate chronic COC would then be 1.23 µg/L; even using a less conservative ACR of 10 plus an assessment factor of 10, the chronic COC would be 12.3 µg/L.

Nine of the 12 discharging facilities for which EPA reported data (see Table_Apx C-1, p. 91) would exceed a chronic COC of 1.23 µg/L. One facility in Pensacola, FL (PALL CORP), with modeled levels as high as 467.92 µg /L – exceed the chronic COC by a factor of 380.

Of note, EPA's summary on p. 47 only refers to a value of 11 µg/L for the chronic exposure scenario. This is inconsistent with Table APX C-1 (p. 91), which includes a value of 10.75 µg/L (which EPA presumably rounded to 11) for one facility (Wilmington, NC) – but also a number of other concentrations well exceeding this value.

Even using a less conservative chronic COC of 12.3 µg/L, five of the 12 discharging facilities would still exceed the chronic COC, by as much as 38-fold (see Table Apx C-1, p. 91).

EPA relied on its flawed and certainly not conservative analysis to claim "[t]hese values do not exceed the acute and chronic COCs for aquatic organisms (246 µg/L and 1,768 µg/L, respectively) indicating a low risk concern." (p. 47) On this basis EPA indicated it will not further analyze exposures to ecological

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[192] *See* Martin May, et al., *Evaluation of acute-to-chronic ratios of fish and Daphnia to predict acceptable no-effect levels*, 28:1 ENVTL. SCIENCES EUROPE (2016), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5044967/; Jan Ahlers, et al., *Acute to chronic ratios in aquatic toxicity - variation across trophic levels and relationship with chemical structure*, 25:11 ENVTL. TOXICOLOGY & CHEMISTRY 2819 (Dec. 2009), 10.1897/05-701R.1. ("For fish, daphnids, and algae, acute to chronic ratios (ACRs) have been determined from experimental data regarding new and existing chemicals. Only test results in accord with the European Union Technical Guidance Document (TGD) and validated by authorities were considered. Whereas the median ACRs of 10.5 (fish), 7.0 (daphnids), and 5.4 (algae) are well below the ACR safety factor of 100 as implied by the TGD, *individual ACRs vary considerably and go up to 4400. The results suggest that a safety factor of 100 is not protective for all chemicals and trophic levels.* Neither a correlation between ACR and baseline toxicity as modeled through the logarithmic octanol-water partition coefficient nor an ACR correlation across trophic levels exists. Narcosis is associated with a preference for a low ACR; nevertheless, low ACRs are frequently obtained for nonnarcotics. Analysis of chemical structures led to the derivation of structural alerts to identify compounds with a significantly increased potential for a high ACR, which may prove to be useful in setting test priorities. *At present, however, life-cycle tests are the only way to conservatively predict long-term toxicity.*") (emphases added).

receptors, including fish, aquatic invertebrates and algae, from NMP release to surface water. EPA later took this conclusion further: "EPA's *conservative* assessment of this exposure scenario predicted NMP surface water concentrations that are well below the hazard benchmarks identified for humans and aquatic organisms." (p. 48, emphasis added)

In contrast to EPA's assertion, the analysis is anything but conservative and is flawed. This pathway certainly warrants additional analysis. EPA should obtain additional information on which to base its COCs and then analyze this pathway further.

B. Occupational exposure via inhalation route

Under its Analysis plan, EPA implies that it may rely in its risk evaluation on the recommended exposure guidelines established by American Industrial Hygiene Association (AIHA) in estimating occupational exposure:

> OSHA has not established any occupational exposure limits for NMP; however, AIHA has adopted a recommended workplace environmental exposure level (WEEL) of 10 ppm based on a time-weighted average (TWA) over an 8-hour workday. EPA will consider the influence of the recommended exposure guidelines in its occupational exposure assessment. (p. 57)

Any assumption of compliance with the WEEL would underestimate exposure. As recommended exposure guidelines are not enforceable, they are unlikely to be routinely followed. For example, the 2015 NMP risk assessment cited a WHO report that found occupational exposures to NMP from paint stripping could be as high as 64 mg/m^3 (or 16 ppm) for an 8-hour time weighted average (TWA) and 280 mg/m^3 (or 69 ppm) for 1 hour peak samples. Further, EPA's Supplemental Consumer Exposure and Risk Estimation Technical Report for NMP in Paint and Coating Removal estimated consumer exposure to be as high as 540.1 mg/m^3 (or 133.2 ppm) for an 8-hour TWA for one scenario ("Floors, Spray Application in Workshop, Windows Open").[193] These values range from 1.6 to 13.3 times higher than the WEEL.

EPA is charged with evaluating real-world exposures and should not assume compliance with voluntary exposure guidelines.

In addition, the inadequacy of the WEEL as sufficiently protective of worker health is illustrated by the lower exposures called for by others. EPA recommended an existing chemical exposure limit (ECEL) as a

[193] U.S. EPA, *Supplemental Consumer Exposure and Risk Estimation Technical Report for NMP in Paint and Coating Removal* at 51 (Nov. 2016), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0231-0199.

more current benchmark for workplace exposures;[194,195] this recommended value (20 mg/m^3, or 4.9 ppm, 8-hour time weighted average), is significantly lower than the WEEL. And the California Department of Public Health recently set a PEL of 1 ppm.[196]

50. EPA's proposed tiered assessment for consumer uses raises concerns.

In its Analysis Plan, EPA explains that it intends to use a tiered approach to assess consumer exposure:

> Evaluate consumer exposures to products and articles containing NMP. The 2015 NMP Risk Assessment for Paint Removal Use provides an in-depth characterization of paint removal products, including the NMP content, use patterns and associated exposures that may occur via their use. During risk evaluation, EPA will consider these paint removal uses along with other consumer uses to conduct a first-tier exposure analysis. The results of this analysis will then be used to determine which consumer use scenarios may need a more refined exposure assessment. In addition to the comparison of consumer exposure scenarios to each other, the associated exposure estimates for each scenario will also be compared to the hazard benchmarks identified for dermal and inhalation exposure. Based on the results of this evaluation, EPA may consider a subset of consumer use scenarios for a more extensive analysis. (p. 58)

TSCA requires EPA to "conduct risk evaluations *** to determine whether a chemical substance presents an unreasonable risk of injury to health or the environment *** *under the conditions of use*." TSCA § 6(b)(4)(A) (emphasis added). EPA must analyze all consumer uses in order to know whether the use itself presents risk.

We have raised concerns throughout these comments about EPA's decision "not to further analyze" exposure pathways based on limited data and questionable assumptions. The same concern applies prospectively. In its first-tier assessment of consumer uses, EPA needs to have a robust scientific basis for deciding not to further refine the exposure analysis for a particular condition of use, including sufficient information as well as justified and documented assumptions. If EPA does not have empirical data (after using its authorities to obtain it), it should use reasonable worst-case assumptions to assure that the first-tier analysis is adequately conservative. Failing to conduct a robust exposure analysis would be inconsistent with the best available science requirement under TSCA section 26(h).

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[194] Memorandum from Chris Brinkerhoff, et al., US EPA Risk Assessment Div., to Niva Kramek, U.S. EPA Chemical Control Div., Recommendation for an Existing Chemical Exposure Limit (ECEL) for Occupational Use of NMP and Workplace Air Monitoring Methods for NMP (Jan. 6, 2016), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0231-0238.

[195] Methylene Chloride and N-Methylpyrrolidone; Regulation of Certain Uses Under TSCA Section 6(a), 82 Fed. Reg. 7464, 7532 (proposed Jan. 19, 2017), https://www.regulations.gov/docket?D=EPA-HQ-OPPT-2016-0231.

[196] Cal. Dep't of Pub. Health, N-Methylpyrrolidone (NMP) (June 2014), https://www.cdph.ca.gov/Programs/CCDPHP/DEODC/OHB/HESIS/CDPH%20Document%20Library/nmp.pdf.

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51. EPA's problem formulation contains statements relating to confidential business information (CBI) that are or may be inconsistent with its authorities and obligations under TSCA.

First, EPA states: "EPA may consider any relevant confidential business information (CBI) in the risk evaluation in a manner that protects the confidentiality of the information from public disclosure." (p. 53) This statement ignores the major changes made to the CBI provisions of TSCA section 14. Companies must substantiate most claims for CBI protection and EPA must review many of them within 90 days of submission of the information. Any claim that does not meet all applicable requirements cannot be protected from disclosure.

EPA later makes an even more absolute statement in the context of human health studies:

> Human health studies will be evaluated using the evaluation strategies laid out in the supplemental document, *Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018). Human and animal data will be identified and included as described in the inclusion and exclusion criteria in Appendix G. *** Further, ***EPA will consider any relevant CBI in a manner that protects the confidentiality of the information from public disclosure***. (p. 59, emphasis added)

Health and safety studies are expressly not eligible for protection as CBI under TSCA, subject only to two very narrow exceptions. *See* 15 U.S.C. § 2613(b)(2). All such information not subject to the exceptions needs to be made public.

Comments on Perchloroethylene

52. EPA has unreasonably excluded from the risk evaluation certain exposures to perchloroethylene on the basis of other environmental statutes.

As discussed earlier in these comments (see Section 5), EPA unreasonably excluded exposures to perchloroethylene through air, drinking water, ambient water, biosolids, and disposal pathways. EPA should not exclude those exposures, for the reasons given above.

For additional reasons, EPA's decision to exclude certain exposures is illegal and arbitrary and capricious. For instance, even though EPA excludes exposures through air because of the Clean Air Act, EPA states that the "[g]eneral population inhalation exposure to perchloroethylene in air may result from industrial manufacturing and processing plant fugitive and stack emissions." U.S. EPA, Problem Formulation of the Risk Evaluation for Perchloroethylene (Ethene, 1,1,2,2-Tetrachloro) at p. 46 (May 2018), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0732-0080. EPA must analyze this exposure. Additionally, even though EPA excludes exposures through drinking water because of the Safe Drinking Water Act, EPA states that the general population may ingest perchloroethylene through drinking water, which "enters water supplies through industrial and commercial wastewater and liquid waste streams, sewage sludge land application, wet deposition (rain) and leaching from contaminated soils." (p. 46) EPA has provided no coherent rationale for excluding this exposure.

In particular, EPA needs to consider all reasonably available information and accurately describe "the magnitude of the exposure of human beings to the chemical substance" based on this risk evaluation. 15 U.S.C. § 2605(c)(2)(A)(i). EPA will be unable to fulfill these duties if it excludes some exposures from its analysis. To the extent EPA lacks information on these exposures, EPA should use its information authorities to address the information gaps.

53. EPA has provided insufficient justification for its decision to conduct no further analysis on a number of exposure pathways.

Occupational Exposures: EPA states that it will do no further analysis on any exposures to workers and Occupational Non-users (ONU) during the distribution of bulk shipments of perchloroethylene or the distribution of formulated products with perchloroethylene. (p. 147) The only reason provided is that "[e]xposure will only occur in the event of spills." (p. 147) Exposure from spills, even if infrequent (and EPA does not even suggest spills are infrequent), still contributes to overall exposure and should be included in the risk evaluation. In addition, distribution includes storage, transfer and transport of perchloroethylene, each of which can entail routine as well as accidental releases through, for example, fugitive emissions, venting, etc.

For numerous worker and ONU exposures, EPA states that it will do no further analysis on mists as an exposure pathway because "mist generation not expected." (pp. 143-56) EPA has provided no explanation, analysis or citation to evidence to support this expectation.

EPA also plans to do no further analysis on dermal exposures from liquid to ONU because "[d]ermal exposure is expected to be primarily to workers directly involved in working with the chemical." (pp. 143-56) TSCA provides no basis for limiting EPA's risk consideration only to intentional exposures, nor to focus only on persons "primarily" exposed.

Consumer Exposures: EPA must analyze all exposures to consumers and bystanders. EPA states that it will not further evaluate the oral pathway for consumers because such exposure "will be limited by a combination of dermal absorption and volatilization." (p. 57) EPA points to no data or analysis supporting this conclusion, and even if this exposure is limited, it will add to the total exposure level. EPA needs to evaluate the oral pathway for consumers. In particular, as EPA acknowledged "[i]nfants and young children may also be exposed to perchloroethylene via mouthing of treated products and articles (e.g., spot treatment of carpets; dry cleaned blanket)." (p. 46) Given the greater likelihood of oral exposure for infants and young children, EPA must analyze these potential exposures.

EPA also states that because bystanders are not directly handling perchloroethylene, "inhalation exposure to mists *** are not expected for bystanders," (p. 46), but this statement does not make sense. A bystander could easily inhale mists even if she is not personally handling the perchloroethylene. EPA points to no evidence supporting this statement. It lacks a factual or rational basis.

EPA states that it will not analyze exposure to consumers from disposal of consumer products because it is anticipated that most products will be disposed of in original containers. (p. 57) Does EPA have any evidence supporting this assumption? And even if disposed of in original containers, does EPA have a plan to evaluate the exposures that eventually flow from this disposal? The problem formulation fails to address these important questions.

When setting forth inclusion criteria for data sources for exposures to consumers and ecological receptors, EPA appears to limit its analysis to sources involving "non-closed systems," thus excluding all sources from "closed systems." (p. 164) EPA has not explained, let alone provided measurable criteria for, what qualifies as a "closed system" for these purposes; EPA should not exclude these data sources on this basis unless the data source reliably confirms that there are no (i.e., zero) exposures to consumers and ecological receptors.

54. EPA should analyze all reasonably available information about the hazards associated with perchloroethylene.

For the reasons articulated earlier in these comments (see Section 1), EPA must consider all reasonably available information about a chemical's hazards when preparing a risk evaluation. *See* 15 U.S.C. § 2625(k). EPA's problem formulation for perchloroethylene suggests that EPA will fail to consider all reasonably available information about both health and environmental hazards.

EPA's plan to analyze human health hazards states that EPA does not plan to evaluate "case reports and series or ecological studies for endpoints that appear to be less severe endpoints (e.g., nausea)." (p. 74) EPA has provided no basis for ignoring this reasonably available information about hazard. It has no basis in the statute. Accurately evaluating the risk presented by a chemical requires consideration of the numerous hazards it presents, and Congress contemplated that, based on the risk evaluation, EPA would be able to describe "the effects of the chemical substance or mixture on health." 15 U.S.C. § 2605(c)(2)(A). Nothing in the statutory text suggests that EPA can ignore certain effects just because they are less severe. Moreover, "less severe" presents an unclear standard for application. How severe does an endpoint need to be for EPA to consider it? EPA needs to fulfill its statutory duty and consider this reasonably available information about hazard.

EPA's plan to analyze environmental hazards appears to potentially be limited to analyzing hazards to aquatic species. (pp. 74-75) EPA needs also to consider hazards to terrestrial species and other ecological receptors. As EPA acknowledges elsewhere in the problem formulation: "Terrestrial species populations living near industrial and commercial facilities using perchloroethylene may be exposed via multiple routes such as ingestion of surface waters and inhalation of outdoor air. As described in Section 2.3.3, perchloroethylene is present and measurable through monitoring in a variety of environmental media including ambient and indoor air, surface water and ground water." (p. 43); *see also* (p. 40) ("Perchloroethylene has been found in *** terrestrial organisms."). Alternatively, it may be that EPA intends to analyze hazard to terrestrial species, but it is not clear that EPA has sufficient information to evaluate those hazards. If EPA lacks sufficient information to characterize the hazards presented to non-aquatic ecological receptors, then EPA should use its information authorities to obtain the reasonably available information regarding these hazards.

55. EPA should analyze the risks to the general population, children, infants, pregnant women, women and men of child-bearing age, and those residing in buildings where dry cleaning occurs.

EPA states that it will not analyze general population exposures to perchloroethylene because EPA considers its existing regulatory programs sufficient. (p. 73) EPA's approach is illegal for the reasons given earlier in these comments (see Section 5). In addition, the reasonably available information establishes that the general population experiences significant exposures to perchloroethylene, and it is irrational to ignore those exposures in light of this evidence. "A subset of National Health and Nutrition Examination Survey (NHANES) data (1999-2000) reported in Lin et al. (2008) show the presence of perchloroethylene in 77% of human blood samples from non-smoking U.S. adults." (p. 42) Perchloroethylene also is a common contaminant in air, soil, surface water, and drinking water, and EPA cannot ignore those exposures which are occurring under its existing regulatory regimes.

Similarly, EPA has identified reproductive/developmental toxicity as a hazard presented by perchloroethylene, and EPA must therefore consider infants, children, pregnant women, and women and men of childbearing age as potentially susceptible subpopulations. (p. 52) "Studies of tetrachloroethylene exposure in humans have evaluated several reproductive outcomes including effects on menstrual disorders, semen quality, fertility, time to pregnancy, and risk of adverse pregnancy outcomes including spontaneous abortion, low birth weight or gestational age, birth anomalies, and

stillbirth (U.S. EPA, 2012e). Data from animal studies identified various manifestations of developmental toxicity." (p. 52)

Given EPA's findings about developmental and reproductive toxicity, infants, children, pregnant women, and women and men of childbearing age are potentially susceptible subpopulations for perchloroethylene under TSCA § 3(12). 15 U.S.C. § 2602(12). TSCA § 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to *** greater susceptibility *** may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." (p. 52) Due to the hazards presented by perchloroethylene, these subpopulations are at greater risk of adverse health effects. There can be no question that each of them is a "relevant" subpopulation for this evaluation.

EPA did not commit to analyzing risks to these subpopulations, despite recognizing these hazards. EPA stated that the available data are "insufficient to allow for a quantitative assessment of the impact of susceptibility on risk." (p. 53) EPA should use its information authorities to generate and obtain the necessary information to prepare the required analysis.

Moreover, available data indicate that a particularly exposed subpopulation would include those residing in buildings where dry cleaning is carried out. "[S]ampling (over 100 samples) of air in six residential apartments in two buildings where dry cleaning was carried out on the ground floor revealed tetrachloroethene concentrations ranging from 50 to 6100 $\mu g/m^3$, with means ranging from 358 to 2408 $\mu g/m^3$." (p. 38) EPA needs to analyze risks to this subpopulation as well due to its greater exposure.

56. EPA should use its information authorities to fill information gaps revealed by the perchloroethylene problem formulation.

In a number of places, EPA appears to use models, surrogate chemicals, or other estimates instead of measured data. EPA should use its various information authorities to obtain actual measured data on perchloroethylene instead of relying so extensively on estimated information. In addition, in places EPA suggests that available information is insufficient for certain portions of the analysis. EPA needs to use its information authorities to fill those information gaps.

EPA's analysis of environmental fate appears to rely overwhelmingly on EPI Suite and other models, not measured evidence. (pp. 35-37) EPA notes that "the literature review is currently underway through the systematic review process," (p. 35) but elsewhere (p. 160), EPA suggests that "environmental fate data will not be further evaluated." EPA should obtain and rely on needed measured data, and EPA should not exclude environmental fate data from its systematic review or its further analysis in the risk evaluation.

EPA also appears to intend to rely heavily on models for both occupational and consumer exposures, but instead EPA should rely on its information authorities to obtain measured information on these exposures. EPA states that: "If measured values resulting from sufficiently high-quality studies are not available (to be determined through the systematic review process), chemical properties will be

estimated using EPI Suite, SPARC, and other chemical parameter estimation models. Estimated fate properties will be reviewed for applicability and quality." (pp. 66-67) Similarly, EPA states that it may use information for surrogate chemicals. (p. 66) Rather than shift immediately to models and surrogates, EPA should use its information authorities to obtain or generate the necessary high-quality studies. EPA's statement in its response to comments (EPA's Responses to Public Comments Received on the Scope Documents for the First Ten Chemicals for Risk Evaluation under TSCA p.13, *available at* https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0725-0051) that available information is sufficient for the risk evaluations cannot be reconciled with EPA's repeated acknowledgement that it may have to rely on models and surrogates in the absence of measured data.

Similarly, EPA stated that "Perchloroethylene specific formulation processes were not identified so EPA will rely on [Emission Scenario Documents (ESDs), Generic Scenarios (GS)]." (p. 108) EPA could obtain this information by exercising its information authorities, and EPA should do so.

It would be particularly appropriate for EPA to use its information authorities to obtain information about the scenarios where EPA was not able to identify applicable Emission Scenario Documents (ESDs), Generic Scenarios (GS), or release scenarios. (pp. 66-67) "EPA was not able to identify ESDs or GSs corresponding to several conditions of use, including use of perchloroethylene as an intermediate, recycling of perchloroethylene, use of perchloroethylene as an industrial processing aid, and use of perchloroethylene in commercial carpet cleaning." (pp. 66-67) EPA needs to use its information authorities to fill these information gaps. In particular, EPA needs accurate information about recycling processes because, according to the TRI data cited in the problem formulation, over 46 million pounds of perchloroethylene are recycled per year, representing over 71% of total waste managed. (p. 39)

As explained earlier in these comments (see Section 6), EPA should not assume that all occupational exposures meet the existing regulatory limits for perchloroethylene. Among other things, the exposure information reveals that some exposures exceed the regulatory and non-regulatory exposure limits identified by EPA. *E.g.*, *compare* (p. 123) (showing maximum 8-hr TWA Concentration of 390 ppm), *with* (p. 44) (describing various regulatory exposure limits well below those levels).

Moreover, EPA indicates that it "was not able to identify occupational exposure scenarios corresponding to several conditions of use due generally to a lack of understanding of those conditions of use (e.g., use of perchloroethylene metal and stone polishes). EPA will perform targeted research to understand those uses which may inform identification of occupational exposure scenarios." (p. 71) EPA must ensure that it has sufficient information to analyze these exposure scenarios, and should use its information authorities to do so.

EPA should also use its information authorities to determine the extent to which exposure occurs through the consumption of fish. EPA acknowledges that the EU Risk Assessment indicates that perchloroethylene may be present in fish, (p. 47), and given widespread contamination of surface water, this source of exposure should be examined. EPA states "EPA does not anticipate fish ingestion to be a significant general population exposure pathway, as perchloroethylene has a low bioaccumulation

potential in aquatic organisms," (p. 47), but given there is evidence to the contrary, EPA must assess the available information to see if the factual record supports this "anticipation."

57. EPA must identify and explain any deviations from its previous assessments of perchloroethylene.

EPA states in the problem formulation:

> Perchloroethylene has an existing EPA IRIS Assessment U.S. EPA (2012e) and a draft ATSDR Toxicological Profile (ATSDR, 2014); hence, many of the hazards of perchloroethylene have been previously compiled. EPA expects to use these previous analyses as a starting point for identifying key and supporting studies to inform the human health hazard assessment, including dose-response analysis. (p. 51)

EPA identifies two previous assessments of perchloroethylene: the IRIS 2012 toxicological review and the 2014 ATSDR toxicological review. The agency further indicates that many of perchloroethylene's hazards were compiled in the ATSDR profile and IRIS toxicological review. Both documents were peer reviewed by independent scientists. EPA has previously relied heavily on IRIS toxicological reviews to develop subsequent risk assessments.

Given EPA's clear indications of the scientific rigor of IRIS toxicological reviews as well as its decision to rely upon them, EPA must identify, explain and justify any deviations from the earlier review in its draft risk evaluation in terms of hazard identification and dose-response characterization. Any differences must be based on compelling scientific evidence and explicitly interrogated through the peer review process.

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Comments on Trichloroethylene

58. EPA should finalize its proposed bans of TCE under TSCA immediately and not use the larger ongoing risk evaluation of TCE as a reason for delay.

EDF incorporates by reference its comments on EPA's proposed rules to ban TCE for use in vapor degreasing, aerosol degreasing, and spot cleaning in dry cleaning facilities.[197,198] EPA's 2014 risk assessment and supplemental technical reports make clear that TCE, under the conditions of use subject to the proposed rules, presents an unreasonable risk of injury to health of workers, occupational bystanders, and consumers. These evaluations reflect input from numerous and extensive peer reviews, incorporate the best available science, and apply a weight-of-the-scientific-evidence approach.

The Lautenberg Act clearly intended for EPA to move forward to address risks it identified in assessments completed prior to enactment.

Section 26(l)(4) states (emphases added):

> (4) CHEMICAL SUBSTANCES WITH COMPLETED RISK ASSESSMENTS.—With respect to a chemical substance listed in the 2014 update to the TSCA Work Plan for Chemical Assessments for which the Administrator has *published a completed risk assessment prior to the date of enactment* of the Frank R. Lautenberg Chemical Safety for the 21st Century Act, the Administrator *may publish proposed and final rules under section 6(a)* that are consistent with the scope of the completed risk assessment for the chemical substance and consistent with other applicable requirements of section 6.

Section 26(p)(3) states (emphasis added):

> (3) ACTIONS COMPLETED PRIOR TO COMPLETION OF POLICIES, PROCEDURES, AND GUIDANCE. – *Nothing in this Act requires the Administrator to revise or withdraw a completed risk evaluation, determination, or rule* under this Act solely because the action was completed prior to the development of a policy, procedure, or guidance pursuant to the amendments made by the Frank R. Lautenberg Chemical Safety for the 21st Century Act.

These provisions of the law make abundantly clear that EPA can proceed to promulgate a rule based on its completed TCE Work Plan risk assessment and is under no obligation to withdraw its prior risk assessment, risk determination or proposed rule. Indeed, Congress included these provisions for the very purpose of grandfathering-in the Work Plan risk assessments EPA had completed and ensuring its authority to use those assessments as the basis for section 6 risk management rules.

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[197] EDF Comments on Trichloroethylene (TCE); Regulation of Use in Vapor Degreasing Under TSCA Section 6(a) (May 19, 2017), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0387-0696.
[198] EDF Comments on Trichloroethylene; Regulation of Certain Uses Under TSCA § 6(a) (Mar. 16, 2017), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0163-0172.

It is indefensible for EPA to delay critically needed action on TCE, as EPA now plans to do, reevaluating those conditions of use in the current risk evaluation. This approach will effectively delay action for years, putting public health at risk. EPA needs to expeditiously finalize its proposed bans of these high-risk uses of TCE, while taking into consideration any exposures remaining from those conditions of use due, for example to allowed exemptions.

59. EPA's apparent intent to deviate from longstanding agency-wide guidance on assessing risks for developmental toxicity lacks scientific justification.

EPA states in the problem formulation document:

> Based on initial screening, EPA plans to analyze the hazards of TCE identified in the scope document. However, when conducting the risk evaluation, the relevance of each hazard within the context of a specific exposure scenario will be judged for appropriateness. *For example, hazards that occur only as a result of chronic exposures may not be applicable for acute exposure scenarios.* This means that it is unlikely that every hazard identified in the scope document will be considered for every exposure scenario.

U.S. EPA, Problem Formulation of the Risk Evaluation for Trichloroethylene at p. 39 (emphasis added) (May 2018), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0737-0083. EPA's proposal here is deeply concerning, and suggests that the agency plans to ignore its own established guidance[199] on the evaluation of chemical hazards and risks. With regard to TCE, EPA's 2011 Integrated Risk Information System (IRIS) assessment[200] correctly identified fetal cardiac malformation, a developmental toxicity effect, as the most sensitive endpoint and supported by multiple lines of evidence—epidemiological, laboratory animal, metabolism, and mechanistic studies. EPA OCSPP reaffirmed this conclusion in its 2014 TCE work plan risk assessment.[201] The TCE problem formulation introduces the possibility that EPA may exclude developmental toxicity as an acute effect—a decision that would not only be odds with EPA's past assessments, proposed regulations, and guidance but also at odds with applying a health-protective approach to chemical risk evaluation.

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[199] *See* U.S. EPA, *Guidelines for Developmental Toxicity Risk Assessment* (Dec. 1991), https://www.epa.gov/sites/production/files/2014-11/documents/dev_tox.pdf.

[200] U.S. EPA, *Toxicological Review of Trichloroethylene (CAS No. 79-01-6) In Support of Summary Information on the Integrated Risk Information System (IRIS)* (Sept. 2011), https://cfpub.epa.gov/ncea/iris/iris_documents/documents/toxreviews/0199tr/0199tr.pdf.

[201] U.S. EPA, *TSCA Work Plan Chemical Risk Assessment Trichloroethylene: Degreasing, Spot Cleaning and Arts & Crafts Uses* (June 2014), https://www.epa.gov/sites/production/files/2014-11/documents/tce_opptworkplanchemra_final_062414.pdf.

As described in EPA's proposed section 6 TCE rules[202,203] and in the 2014 TCE risk assessment, EPA relied on developmental endpoints for assessing health risks of TCE resulting from acute exposure. This is in alignment with EPA's longstanding agency-wide guidance, Guidelines for Developmental Toxicity Risk Assessment,[204] which indicates that even a single exposure to a chemical within a critical window of development may produce adverse developmental effects. For example, EPA's proposed section 6 TCE rule, Trichloroethylene (TCE) Regulation of Use in Vapor Degreasing Under TSCA Section 6(a), states:

> As indicated in the TCE risk assessment, EPA's policy supports the use of developmental studies to evaluate the risks of acute exposures. This science-based policy presumes that a single exposure of a chemical at a critical window of fetal development may produce adverse developmental effects (Ref. 5). This is the case with cardiac malformation. EPA reviewed multiple studies for suitability for acute risk estimation including a number of developmental studies of TCE exposure and additional developmental studies of TCE metabolites (Appendix N) (Ref. 2). EPA based its acute risk assessment on the most sensitive health endpoint (*i.e.,* fetal heart malformations) representing the most sensitive human life stage (*i.e.,* the developing fetus) (Ref. 2).[205]

As a general matter, EDF strongly recommends that EPA follow this established EPA risk assessment practice, and include developmental toxicity effects in its assessment of acute exposure from chemicals. In the case of TCE, EDF strongly recommends that the agency include fetal cardiac malformations in its assessment of acute effects in addition to its assessment of chronic effects. EPA has provided no basis for deviating from this practice in its problem formulation, and to do so would deviate from using the best available science as required under TSCA.

60. EPA's problem formulation raises concerns regarding the agency's approach to the evaluation of fetal cardiac malformations.

In the "Human Health Hazards" section of the Analysis Plan, EPA states:

> The final TSCA Work Plan Chemical Risk Assessment of TCE (U.S. EPA, 2014c) included an assessment of fetal cardiac malformations. EPA will use the systematic review approach (U.S. EPA, 2018) to re-evaluate key studies in this assessment as well as more recent information on this endpoint. of mechanistic data as part of EPA's reevaluation of key

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[202] Trichloroethylene; Regulation of Certain Uses Under TSCA § 6(a), 81 Fed. Reg. 91592, 91595, 91599 (proposed Dec. 16, 2016), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0163-0001.
[203] Trichloroethylene (TCE); Regulation of Use in Vapor Degreasing Under TSCA Section 6(a), 82 Fed. Reg. 7432, 7435, 7439 (proposed Jan. 19, 2017), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0387-0001.
[204] U.S. EPA, *Guidelines for Developmental Toxicity Risk Assessment* at 4, 45 (Dec. 1991), https://www.epa.gov/sites/production/files/2014-11/documents/dev_tox.pdf.
[205] Trichloroethylene (TCE); Regulation of Use in Vapor Degreasing Under TSCA Section 6(a), 82 Fed. Reg. 7432, 7439 (proposed Jan. 19, 2017), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0387-0001.

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> studies. [*sic*] Mechanistic data related to all other endpoints will be identified as "Supplemental Information." (p. 68)

In response to EDF's request for a correction of the typo in this excerpt, EPA indicated the excerpt should read as follows:

> The final TSCA Work Plan Chemical Risk Assessment of TCE (U.S. EPA, 2014c) included an assessment of fetal cardiac malformations. EPA will use the systematic review approach (U.S. EPA, 2018) to re-evaluate key studies in this assessment as well as more recent information on this endpoint. ~~of mechanistic data as part of EPA's reevaluation of key studies.~~ Mechanistic data related to all other endpoints will be identified as "Supplemental Information. [206]
>
> [AND]
>
> Mechanistic data related to developmental toxicity in general is included in the PECO statement for our systematic review. Mechanistic data for non-developmental toxicity will be considered supplemental for the time being.[207]

EPA indicates in its *Application of Systematic Review in TSCA Risk Evaluations* document (hereafter "TSCA Systematic Review document"):[208]

> EPA/OPPT plans to prioritize the evaluation of mechanistic evidence instead of evaluating all of the identified evidence upfront. This approach has the advantage of conducting a focused review of those mechanistic studies that are most relevant to the hazards under evaluation. The prioritization approach is generally initiated during the data screening step. For example, many of the human health PECOs [Populations Exposures Comparators and Outcomes] for the first ten TSCA risk evaluation [*sic*] excluded mechanistic evidence during full text screening. Excluding the mechanistic evidence during full text screening does not mean that the data cannot be accessed later. The assessor can eventually mine the database of mechanistic references when specific questions or hypotheses arise related to the chemical's MOA [mode of action]/AOP [adverse outcome pathway].[209]

Taken together, these excerpts suggest EPA intends to treat the scientific evidence for fetal cardiac malformations and for developmental toxicity generally differently than it will other endpoints. Yet it provides no rationale for doing so. EPA has not explained why it is treating mechanistic data pertaining to fetal cardiac malformations and developmental toxicity differently from all other endpoints. Such a decision in the absence of a scientific explanation is inappropriate especially within a systematic review

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[206] Personal communication from Niva Kramek (EPA) to Jennifer McPartland (July 12, 2018).
[207] Personal communication from Keith Jacobs (EPA) to Jennifer McPartland (July 12, 2018).
[208] U.S. EPA, *Application of Systematic Review in TSCA Risk Evaluations* (May 2018), https://www.epa.gov/sites/production/files/2018-06/documents/final_application_of_sr_in_tsca_05-31-18.pdf.
[209] *Id.* at 172.

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framework, and more broadly serves to highlight the serious problems that arise from the absence of a protocol.[210] EPA's unreasoned dissimilar treatment of similar information is arbitrary and capricious.

61. EPA has failed to describe how it will evaluate non-quantitative data for contribution to weight of evidence, and qualitative endpoints that are not appropriate for dose-response assessment.

In describing how it expects to analyze TCE's human health hazards, EPA states: "Non-quantitative data will also be evaluated for contribution to weight of evidence or for evaluation of qualitative endpoints that are not appropriate for dose-response assessment." (p. 69). EPA provides no further explanation.

EPA fails to describe how it intends to evaluate non-quantitative data for contribution to weight of evidence, or for qualitative endpoints that are not appropriate for dose-response assessment. EPA's TSCA Systematic Review document also fails to provide this detail.

62. EPA statements calling for reevaluating the available science pointing to TCE health risks are vague and insufficiently supported, with no clear next step identified.

In the problem formulation EPA states:

> Human health hazards from acute and chronic exposures will be identified by evaluating the human and animal data that *meet the systematic review data quality criteria* described in the Application of Systematic Review in TSCA Risk Evaluations (U.S. EPA, 2018) document. Data quality evaluation will be performed on key studies identified from the Integrated Risk Information System (IRIS) Toxicological Review of TCE (U.S. EPA, 2011c), the final TSCA Work Plan Chemical Risk Assessment of TCE (U.S. EPA, 2014c) and studies published after 2010 that were captured in the comprehensive literature search conducted by the Agency for TCE [Tricholoroethylene (79-01-6) Bibliography: Supplemental File for the TSCA Scope Document; (EPA-HQ-OPPT-2016-0737; U.S. EPA, 2017g)]. Hazards identified by studies *meeting data quality criteria* will be grouped by routes of exposure relevant to humans (oral, dermal, inhalation) and by cancer and noncancer endpoints. (p. 69, emphases added)

EPA has not explained, either here or in its TSCA Systematic Review document, what it means for data or studies to "meet the systematic review data quality criteria." EPA has also not explained what it means by "key studies," including how they will be identified from the IRIS toxicological review, Work Plan Chemical Risk Assessment, and post-2010 literature review and how they will be used in the risk evaluation.

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[210] *See* EDF Comments on Application of Systematic Review in TSCA Risk Evaluation, https://www.regulations.gov/docket?D=EPA-HQ-OPPT-2018-0210 (to be posted in the docket link provided).

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63. EPA should rely on its prior hazard assessment in the current risk evaluation, and identify and justify any deviations from it.

EPA states in the problem formulation:

> TCE has an existing EPA IRIS Assessment (U.S. EPA, 2011c) and an ATSDR Toxicological Profile (ATSDR, 2014a); hence, many of the hazards of TCE have been previously compiled and systematically reviewed. Furthermore, EPA previously reviewed data/information on health effects endpoints, identified hazards and conducted dose-response analysis in the TSCA Work Plan Chemical Risk Assessment of TCE (U.S. EPA, 2014c). EPA has relied heavily on these comprehensive reviews in preparing this problem formulation. EPA expects to use these previous analyses *as a starting point for identifying key and supporting studies* to inform the human health hazard assessment, including dose-response analysis. The relevant studies will be evaluated using the data quality criteria in the Application of Systematic Review in TSCA Risk Evaluations document (U.S. EPA, 2018). (p. 44, emphasis added)

The agency indicates that "many of the hazards of TCE have been previously compiled and systematically reviewed," which was in fact done in the ATSDR profile and the IRIS toxicological review. EPA should heavily rely on its IRIS assessment, which is based on the best available science and has been peer reviewed. As noted in EPA's Work Plan assessment, EPA relied heavily on the IRIS toxicological review to develop the Work Plan assessment. In describing the IRIS toxicological review, EPA stated in the Work Plan Assessment:

> The assessment uses the hazard and dose-response information published in the final toxicological review that the U.S. EPA's Integrated Risk Information System (IRIS) published in 2011 (EPA, 2011e). The TCE IRIS assessment used a weight-of-evidence approach, the latest scientific information and physiologically-based pharmacokinetic (PBPK) modeling to develop hazard and dose-response assessments for TCE's carcinogenic and non-carcinogenic health effects resulting from lifetime inhalation and oral exposures. In addition to relying on the latest scientific information, the TCE IRIS assessment underwent several levels of peer review including agency review, science consultation on the draft assessment with other federal agencies and the Executive Office of the President, public comment, external peer review by the EPA's Science Advisory Board (SAB) in 2002, scientific consultation by the U.S. National Academy of Sciences (NAS) in 2006, external peer review of the revised draft assessment by the EPA's Science Advisory Board (SAB) in January 2011, followed by final internal agency review and EPA-led science discussion on the final draft.[211]

[211] U.S. EPA, *TSCA Work Plan Chemical Risk Assessment Trichloroethylene: Degreasing, Spot Cleaning and Arts & Crafts Uses* at 20-21 (June 2014), https://www.epa.gov/sites/production/files/2014-11/documents/tce_opptworkplanchemra_final_062414.pdf.

Given EPA's multiple, clear statements affirming the scientific rigor of the IRIS toxicological review as well as its decision to rely upon it in its 2014 Work Plan Assessment[212] and subsequent TSCA section 6 proposed bans, EDF firmly believes that it is unnecessary – not to mention a waste of time and resources – to re-conduct aspects of the agency's previous hazard identification and dose-response characterization unless EPA can demonstrate serious shortcomings in the previous assessment. Further, EPA must identify and explain any decision to deviate from the previous IRIS assessment and clearly identify in its draft risk evaluation any modifications it proposes in hazard identification and dose-response characterization, and the scientific justification for them. Any such differences must be based on compelling scientific evidence and explicitly interrogated through the peer review process.

The excerpt from the problem formulation refers to "key," "supporting," and "relevant" studies. The meaning of these descriptors is entirely unclear. EPA must explicitly define the meaning of these terms and their implications with regard to the agency's approach to systematic review and risk evaluation.

64. EPA fails to acknowledge its previous physiologically-based pharmacokinetic (PBPK) analysis described extensively in its peer-reviewed 2014 Work Plan Chemical Assessment.

In the "Human Health Hazards" section of the Analysis Plan in the problem formulation, EPA states:

> EPA will evaluate whether the available physiologically-based pharmacokinetic (PBPK) and empirical kinetic models are adequate for route-to-route and interspecies extrapolation of the POD, or for extrapolation of the POD to standard exposure durations (e.g., lifetime continuous exposure). If application of the PBPK model is not possible, oral PODs may be adjusted by body weight$^{3/4}$ ($BW^{3/4}$) scaling in accordance with (U.S. EPA, 2011b), and inhalation PODs may be adjusted by exposure duration and chemical properties in accordance with (U.S. EPA, 1994). (p. 69-70).

EPA fails entirely to acknowledge the route-to-route analysis performed as part of the 2014 Work Plan Assessment that was extensively peer reviewed. As noted in the Work Plan Assessment:

> PBPK model—route-to-route extrapolation: PBPK-derived hazard values were based on PODs from either inhalation or oral studies. The TCE PBPK model used interspecies and route-to route extrapolation approaches to convert both the inhalation and oral PODs to human internal doses. Then, the model estimated the human equivalent concentrations needed to produce the human internal doses. Since the PBPK model was

[212] It bears emphasis that extensive peer reviews were undertaken for the IRIS toxicological reviews and 2014 Work Plan assessment. *See* EDF Comments on Trichloroethylene (TCE); Regulation of Use in Vapor Degreasing Under TSCA Section 6(a) at 4, 26 (May 19, 2017), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0387-0696; EDF Comments on Trichloroethylene; Regulation of Certain Uses Under TSCA § 6(a) at 4, 20 (Mar. 16, 2017), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0163-0172.

used, the uncertainties associated with using oral studies for inhalation exposures were minimized.[213]

EDF recommends that EPA use its previous PBPK route-to-route extrapolation approach. Any decision to deviate from the agency's previous PBPK modeling approaches should require a compelling, scientifically-based justification based on empirical evidence.

65. EPA must use its information authorities under TSCA to address areas where there is insufficient information to evaluate risks.

The problem formulation identifies numerous information gaps in evaluating TCE's risks. Examples of such gaps are listed below.

- Table 2-3, *Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation*, includes a category "other uses" within the "industrial/commercial/consumer use" lifecycle stage. Appendix B.1.3.10 describes this "other uses" category as follows:

  > Based on products identified in EPA's Use Document, [EPA-HQ-OPPT-2016-0737-0003 (U.S. EPA, 2017c)], a variety of other uses may exist for TCE, including use in hoof polish, pepper spray and as a toner aide. It is unclear at this time the total volume of TCE used in any of these applications. EPA has not identified any information to further refine the use of TCE in these products at this time; more information on these uses will be gathered through expanded literature searches in subsequent phases of the risk evaluation process. (p. 108)

  Here EPA acknowledges a significant lack of information regarding the "other uses" category of conditions of use. Even still, EPA intends not to use any of its information authorities under TSCA sections 4 and 8 to address these information gaps. Instead, EPA indicates that it will attempt to fill them through an expanded literature search for which there is no assurance EPA will obtain the information it needs. EPA provides no discussion of what action it will take to obtain necessary information if the expanded literature search proves inadequate. Moreover, a decision by EPA to wait to use its information authorities until after the literature search is completed is inefficient and may not provide enough time for EPA to obtain and integrate information into its risk evaluations.

- On page 34 EPA states: "Compared with other environmental media, there is a relative lack of nationally representative monitoring data on levels of TCE in ambient soil." Here again, EPA has identified an information gap that it should fill using its information authorities under TSCA.

[213] U.S. EPA, *TSCA Work Plan Chemical Risk Assessment Trichloroethylene: Degreasing, Spot Cleaning and Arts & Crafts Uses* at 122-23 (June 2014), https://www.epa.gov/sites/production/files/2014-11/documents/tce_opptworkplanchemra_final_062414.pdf.

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- On page 45 EPA states:

> Limited epidemiological data do not support an association between TCE exposure and allergic respiratory sensitization or asthma; however, there is strong human evidence for severe skin sensitization resulting in dermatitis, mucosal lesions and often systemic effects such as hepatitis. Skin sensitization tests on rodents corroborate the contact allergenicity potential of TCE and its metabolites along with the resulting immune-mediated hepatitis (U.S. EPA, 2011c)."

Here EPA appears to be relying on acknowledged limited data to assert a lack of association between exposure and allergic respiratory sensitization or asthma. This is especially problematically given observed linkages between skin sensitization and respiratory sensitization for chemicals.[214] EPA should use its information authorities to obtain additional information about TCE exposure and allergic respiratory sensitization and asthma.

- On page 60 EPA states:

> EPA was not able to identify release scenarios corresponding to several conditions of use, including recycling of TCE, commercial carpet cleaning, and as an industrial process solvent. EPA will perform additional targeted research to understand those conditions of use, which may inform identification of release scenarios. EPA may also need to perform targeted research for applicable models and associated parameters that EPA may use to estimate releases for certain conditions of use.

Here again, EPA acknowledges significant information gaps regarding release scenarios from several conditions of use of TCE. Even still, the agency intends not to use any of its information authorities under TSCA sections 4 and 8. Instead, EPA indicates that it will attempt to fill these information gaps through "additional targeted research" on various conditions of use and applicable models and associated parameters. The meaning of "additional targeted research" is entirely unclear. EPA should define what "additional targeted research" means as a general matter, and immediately initiate use of its information authorities to obtain information necessary to identify the missing release scenarios.

- On page 63 EPA states:

> EPA has identified Emission Scenario Documents (ESDs) from the Organization for Economic Co-operation and Development (OECD) and EPA Generic Scenarios

[214] European Chemicals Agency, Guidance on Information Requirements and Chemical Safety Assessment Chp. R.7a: Endpoint specific guidance (Jul. 2017), https://protect-us.mimecast.com/s/IzjeCpYzmDhnE3g3SPVakj?domain=echa.europa.eu.

> (GS's) corresponding to some conditions of use. For example, the ESD on Industrial Use of Adhesives for Substrate Bonding, the ESD on Metalworking Fluids, and the GS for textile finishing are some of the ESDs and GS's that EPA may use to estimate occupational exposures. EPA will need to critically review these generic scenarios and ESDs to determine their applicability to the conditions of use assessed. EPA was not able to identify ESDs and GSs corresponding to several conditions of use, including manufacture of TCE, use of TCE as an intermediate, recycling of TCE, and commercial carpet cleaning. EPA may conduct industry outreach efforts or perform supplemental, targeted research to understand those conditions of use, which may inform identification of exposure scenarios. EPA will consider inhalation exposure to vapor and mist models in the Chemical Screening Tool for Exposure and Environmental Releases (ChemSTEER) Tool that are routinely used for assessing new chemicals. EPA may also need to perform targeted research to identify applicable models that EPA could use to estimate exposures for certain conditions of use.

EPA must obtain emission information it explicitly acknowledges is lacking for "several conditions of use." EPA indicates it "may conduct industry outreach efforts"—a hardly convincing indication that EPA will actually pursue outreach and that also disregards its information authorities under TSCA. Again, the meaning of "targeted research" is entirely opaque and must be explained.

- In describing its analysis plan for occupational exposure on page 64, EPA states: "EPA anticipates that existing EPA/OPPT dermal exposure models would not be suitable for quantifying dermal exposure to highly volatile chemicals such as TCE."

  If EPA does not have sufficient information on dermal exposure whether through measured or modeled data, it must obtain such information. EPA's indication that dermal exposure models may not be suitable for quantifying dermal exposure is confusing and concerning given the agency's quantification of dermal absorption in early sections of the problem formulation (see for example p. 47). EPA indicates that its exposure models are not suitable and yet provides specific absorption percentages using a specific model, IHSkinPerm. This is entirely incongruent. EPA must obtain sufficient information to accurately assess dermal exposure.

- On pages 64 and 65 EPA states:

> EPA was not able to identify occupational exposure scenarios corresponding to several conditions of use due generally to a lack of understanding of those conditions of use. EPA will perform targeted research to understand those uses which may inform identification of occupational exposure scenarios and analyze those uses identified.

This is yet another example of EPA not using its information authorities while explicitly acknowledging significant information gaps regarding occupational exposures.

66. EPA goes out of its way to avoid using its information authorities in numerous instances.

Throughout the problem formulation EPA goes out of it way to avoid using its information authorities. Examples of such instances are listed below.

- On page 58 EPA states:

> While EPA has conducted a comprehensive search for reasonably available data as described in the Scope for TCE (EPA-HQ-OPPT-2016-0737-0057; U.S. EPA, 2017d), EPA encourages submission of additional existing data, such as full study reports or workplace monitoring from industry sources, that may be relevant for refining conditions of use, exposures, hazards and potentially exposed or susceptible subpopulations during the risk evaluation. EPA will continue to consider new information submitted by the public.

  Rather than relying solely on voluntary submissions—an approach that has proven insufficient in the past[215]—EPA should use its information authorities to obtain necessary information on conditions of use, exposures, hazards, and potentially exposed or susceptible subpopulations.

- On page 59 under the environmental releases section of the analysis plan, EPA states:

> EPA has reviewed key release data sources including the Toxics Release Inventory (TRI). EPA will continue to review relevant data sources as identified in Table_Apx B-4 during risk evaluation. EPA will match identified data to applicable conditions of use and identify data gaps when no data are found. Additionally, for conditions of use where no published release data are available, EPA may use a variety of methods including the application of conservative release estimation approaches and assumptions in the Chemical Screening Tool for Exposures and Environmental Releases (ChemSTEER).

  EPA indicates it will "use a variety of methods" to gather data "where no published release data are available" and uses the ChemSTEER model as the only example of such a method. Again, EPA provides no indication it will use its information authorities even where information gaps exist.

67. EPA is not evaluating potentially exposed or susceptible subpopulations as required under the law.

In the problem formulation EPA identifies potentially exposed or susceptible subpopulations but will not be considering them in the risk evaluation as required under the law. Specifically EPA indicates

[215] *See* section 8; *see also* EDF Comments on § 6(h) PBTs under the Toxic Substances Control Act at 10-13 (Jan. 12, 2018), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0730-0014.

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widespread contamination of TCE in soil and groundwater but will not consider the risks to subpopulations that may be affected by such contamination in the risk evaluation. On pages 33 and 34 EPA notes widespread TCE contamination:

> While the primary fate of TCE released to surface waters or surface soils is volatilization, TCE is more persistent in air and ground water, where it is commonly detected through national and state-level monitoring efforts. TCE is frequently found at Superfund sites as a contaminant in soil and ground water TCE has been detected in ambient air across the United States.

Yet notably absent from EPA's list of potentially exposed or susceptible subpopulations in section 2.3.5.4 are subpopulations that live in proximity to such sources of TCE contamination. EPA's apparent decision to ignore these subpopulations is entirely inconsistent with requirements under TSCA. EPA must include these subpopulations in its risk evaluation of TCE.

68. TCE exposures to terrestrial organisms can occur through multiple pathways of exposure.

EPA is ignoring important pathways of TCE exposures to terrestrial organisms. EPA states:

> Exposure to terrestrial organisms is expected to be low since physical chemical properties do not support an exposure pathway through water and soil pathways to these organisms. The partition of TCE into sediments is very low. Furthermore, the primary fate of TCE released to surface waters or surface soils is volatilization. (p. 35)

This statement ignores entirely TCE exposures to terrestrial organisms through air, which is a primary pathway of exposure to TCE. EPA establishes the case for this throughout the problem formulation document. For example in section 2.2.3, Presence in the Environment and Biota, EPA notes, "TCE is more persistent in the air and ground water, where it is commonly detected through national and state-level monitoring efforts" and "TCE has been detected in ambient air across the United States, though ambient levels vary by location and proximity to industrial activities." (pg. 33)

Additionally, EPA is ignoring exposures to terrestrial organisms that may occur from contaminated water and soil.

EPA must comprehensively consider all routes of exposure to terrestrial organisms in its risk evaluation of TCE given its widespread detection throughout the environment including at contaminated sites.

69. EPA repeatedly only references aquatic plants when describing its approach to evaluating aquatic species.

Throughout the problem formulation document, EPA repeatedly parenthetically references aquatic plants only in "i.e." statements relating to ecological exposures to aquatic species via contaminated surface water. For example:

> EPA expects to analyze aquatic species (i.e., aquatic plants) exposed via contaminated surface water. There are no national recommended water quality criteria for the

> protection of aquatic life for TCE and as a result EPA does not believe that TCE exposure to aquatic organisms in surface water has been adequately assessed. (p. 53)

In doing so, EPA suggests that it will only consider aquatic plants and no other aquatic species in its evaluation of aquatic species exposed via contaminated surface water. EPA must comprehensively consider all relevant aquatic organisms in its assessment of such exposures. If this is unintentional, EPA should change all relevant "i.e." references to "e.g." references. If it is intentional, EPA needs to revise its proposed approach to evaluating aquatic species to include all relevant aquatic species, which extend well beyond aquatic plants.

70. EPA must include exposures to the general population in its risk evaluation of TCE.

EPA has erroneously proposed to ignore exposures to the general population from TCE. For example,

> EPA does not plan to consider and analyze general population exposures in the risk evaluation for TCE. EPA has determined that the existing regulatory programs and associated analytical processes have addressed or are in the process of addressing potential risks of TCE that may be present in various media pathways (e.g., air, water, land) for the general population. For these cases, EPA believes that the TSCA risk evaluation should focus not on those exposure pathways, but rather on exposure pathways associated with TSCA uses that are not subject to those regulatory processes. (p. 63)

EPA's decision to exclude exposures to the general population is unscientific, not health-protective, and illegal. EPA must include the general population in its assessment of TCE, particularly given known inhalation exposures via ambient air and ingestion.[216]

71. EPA's exclusion of non-occluded dermal exposures to workers lacks rationale and is inconsistent with its approach to including occluded dermal exposures.

In describing its approach to evaluating occupational dermal exposures to TCE, EPA states:

> Exposures to skin that are instantaneous would be expected to evaporate before significant dermal exposure would occur based on the physical chemical properties including the vapor pressure, water solubility, and log Kow (the estimate from IHSkinPerm, a mathematical tool for estimating dermal absorption, is 0.8% absorption and 99.2% volatilization). Exposure that occurs as a deposition over time or a repeated exposure that maintains a thin layer of liquid TCE would have greater absorption (the estimate from IHSkinPerm for an 8-hr exposure is 1.6% absorption and 98.4% volatilization). In both instantaneous or repeated exposure scenarios, the dermal exposures to liquid TCE would be concurrent with inhalation exposures and overall the contribution of dermal exposure to the total exposure is relatively small. This is in

[216] U.S. EPA, *Sources, Emission and Exposure to Trichloroethylene (TCE) and Related Chemicals* at 23-26 (Mar. 2001), http://ofmpub.epa.gov/eims/eimscomm.getfile?p_download_id=4824.

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> agreement with the NIOSH skin notation profile for TCE, which estimates a low hazard potential by dermal absorption for systemic effects when inhalation and dermal exposures are concurrent (NIOSH, 2017). Therefore, it is not anticipated that dermal absorption will be significant for the majority of occupational exposure scenarios; thus, non-occluded dermal exposure scenarios will not be analyzed for workers. Based on the 2017 NIOSH Skin Notation Profile for TCE, TCE is associated with systemic and direct (i.e., irritation) effects, as well as sensitization. An occluded exposure scenario, wherein liquid TCE is not able to evaporate readily, may have dermal exposures that significantly contribute to the total exposure or effects on the skin (e.g., dermal sensitization). An example of such an occluded scenario includes TCE being trapped under a worker's glove during occupational activities, thus preventing the rapid volatilization that generally inhibits dermal absorption. Therefore, occluded dermal exposure scenarios will be analyzed for workers. (p. 47)

That a smaller relative percentage of exposure to TCE is expected from dermal versus inhalation exposure does not mean that the dermal exposure is irrelevant to evaluating TCE risks in occupational settings. The contribution of TCE exposure from dermal absorption could be a significant source of exposure in a comprehensive evaluation of TCE's risks. Indeed, in EPA's 2014 Work Plan Assessment, the agency noted:

> Rapid absorption through the skin has been shown by both vapor and liquid TCE contact with the skin. EPA (2011e) summarized several volunteer studies in which both TCE liquid and vapors were shown to be absorbed in humans via the dermal route. Following exposures of between 20 and 30 minutes, absorption was rapid, with peak TCE levels in expired air occurring within 15 minutes (liquid) and 30 minutes (vapor).[217]

EPA should consider combined exposures to TCE via all pathways across all potential sources of exposure.

Moreover, it is not clear why EPA will include occluded dermal exposures to workers but not non-occluded dermal exposure that "maintains a thin layer of liquid." Ostensibly, both exposures scenarios result in continuous dermal contact and absorption of TCE.

72. EPA's approach to evaluating consumer dermal exposure to TCE is problematic and points to inconsistencies in how EPA plans to evaluate dermal occupational exposures.

In describing its approach to evaluating consumer dermal exposures to TCE, EPA states:

> Conceptual model for consumers, dermal exposure: "There is potential for dermal exposures to TCE from consumer uses. As described in section 2.5.1, TCE in direct

[217] U.S. EPA, *TSCA Work Plan Chemical Risk Assessment Trichloroethylene: Degreasing, Spot Cleaning and Arts & Crafts Uses* at 72 (June 2014), https://www.epa.gov/sites/production/files/2014-11/documents/tce_opptworkplanchemra_final_062414.pdf.

> contact with skin would be expected to evaporate before significant dermal absorption could occur. Based on TCE's physical chemical properties, including the vapor pressure, water solubility and log KOW, only 0.8% is expected to be absorbed dermally after instantaneous exposure and only 1.6% of TCE is expected to be absorbed dermally after an 8-hour duration of continual deposition. Furthermore, dermal exposures to liquid TCE are expected to be concurrent with inhalation exposures, which reflect the preponderance of overall exposure from a particular use or activity for most consumer exposure scenarios. Therefore, non-occluded dermal exposure scenarios will not be analyzed for systemic effects for users. However, dermal sensitization will still be considered for these scenarios. There may also be certain scenarios with a higher dermal exposure potential, for example, an occluded scenario where liquid TCE is not able to evaporate readily such as a user holding a rag soaked with liquid TCE against their palm during a cleaning activity. Therefore, occluded dermal exposure scenarios will be evaluated for both systemic effects and sensitization and non-occluded scenarios will only be evaluated for sensitization. In scenarios involving exposure to TCE vapor, inhalation and dermal exposures would also be concurrent, with predominate exposure from inhalation. A dermal to inhalation uptake ratio of around 0.1% for vapor to skin scenarios is predicted using IHSkinPerm. Therefore, only the inhalation exposures will be analyzed in these cases. (p. 50)

As with dermal occupational exposure, EPA's invoking of the relatively smaller percentage of dermal exposure from TCE when compared to inhalation exposure as a basis for excluding most non-occluded dermal exposure scenarios is arbitrary and not a basis for deeming such exposure to be irrelevant to evaluating TCE risks to consumers.

For consumer exposures, EPA is proposing not to examine non-occluded dermal exposure for systemic effects but to include such exposures for sensitization. This decision is inconsistent with EPA's approach to occupational dermal exposures where it does not plan to examine non-occluded dermal exposures for either skin sensitization or systemic effects.

For both occupational and consumer exposures, EPA should include non-occluded and occluded dermal exposure in its risk evaluation for all relevant endpoints.

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Comments on Pigment Violet 29

73. EPA's decision not to further analyze any condition of use for Pigment Violet 29, based on presumed low hazard and exposure potential, is unsupported.

Unlike most of the other problem formulations, EPA does not intend to exclude any conditions of use from the risk evaluation, but EPA also states that it does not plan to conduct further analysis on any condition of use of Pigment Violet 29:

> EPA determined as part of problem formulation that it is not necessary to conduct further analysis on the exposure pathways that were identified in the C.I. Pigment Violet 29 scope document (U.S. EPA, 2017c) and that remain in the risk evaluation.****EPA expects to be able to reach conclusions about particular hazards or exposure pathways without extensive evaluation and plans to conduct no further analysis on those hazards or exposure pathways in order to allow EPA to focus the Agency's resources on more extensive or quantitative analyses. As discussed below, EPA preliminarily determined that there are no environmental release and waste pathways for the environment or general populations that EPA plans to further analyze in the risk evaluation.

U.S. EPA, Problem Formulation of the 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) at pp. 29-30 (May 2018), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0725-0048.

EPA's decision to not further analyze any condition of use for Pigment Violet 29 is not supported based on the limited hazard and exposure information available. More broadly, the problem formulation strongly signals the agency's intent to find that Pigment Violet 29 does not present risks to humans or the environment. Before any risk conclusions can be reached, EPA must obtain significantly more hazard and exposure information on Pigment Violet 29 and integrate such information into a comprehensive evaluation of risk.

EDF recommends that EPA immediately use its information authorities under TSCA to fill information gaps to ensure that the agency has sufficient information to perform a comprehensive and robust risk evaluation of Pigment Violet 29 based on the best available science. As EDF has previously explained, EPA must use its authorities under TSCA §§ 4 and 8 to obtain additional information. EDF incorporates and reiterates those points here as well. EDF Comments on Ten Scopes under the Toxic Substances Control Act pp.11-15, https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0743-0069. As particularly relevant here, EPA must use these information authorities because TSCA orders EPA to consider "available" and "reasonably available" information in crafting a risk evaluation, 15 U.S.C. §§ 2605(b)(4)(F)(i), 2625(k), and under the new risk evaluation rule, EPA defined "[r]easonably available information" to mean "information that EPA possesses or can reasonably generate, obtain, and synthesize for use in risk evaluations, considering the deadlines specified in TSCA section 6(b)(4)(G) for completing such evaluation." 40 C.F.R. § 702.33, promulgated at 82 Fed. Reg. 33,748 (July 20, 2017). Thus, under its own rule, EPA has to consider information that it "can reasonably generate, obtain, and synthesize."

In turn, TSCA § 4(a)(2) provides that EPA "may, by rule, order, or consent agreement require the development of new information relating to a chemical substance *** if the Administrator determines that the information is necessary *** to perform a risk evaluation under section 6(b)." 15 U.S.C. § 2603(a)(2)(A)(i). Congress provided this additional testing authority allowing EPA to require testing or other data development efforts solely upon a determination "that the information is necessary *** to perform a risk evaluation under section 6(b)." *Id.* Here, much additional information is necessary to prepare a risk evaluation for Pigment Violet 29, and EPA must use its authority to fill these information gaps. Congress expressly gave EPA broader testing authority to fill information gaps when preparing risk evaluations, and EPA cannot ignore that authority when it so clearly lacks information necessary for an adequate risk evaluation.

A. The evidence base for Pigment Violet 29 is severely lacking.

In total EPA is relying on three main sources of information for Pigment Violet 29: 1) REACH registration materials, 2) an FDA food additive petition, and 3) estimated data from EPA's EPI Suite program. The majority of the limited information on Pigment Violet 29 comes from the REACH registration materials.

Information available through these sources is captured in the problem formulation appendices C (Physical and Chemical Properties), D (Environmental Fate Studies), E (Environmental Hazard Study Summaries), and F (Human Health Hazard Study Summaries). An overview of the available information is provided in the table below alongside initial concerns raised by the limited information.

Information Type	Number of Studies	Study types	Initial Concerns
Physical and Chemical Properties (Appendix C)[218]	6	OECD 102 (melting point); OECD 104 (vapor pressure); OECD 105 (water solubility); OECD 109 (density); octanol/water coefficient; solubility in n-octanol	
Environmental Fate (Appendix D)[219]	3	OECD 301 F (Biodegradability); OECD 305 (Bioaccumulation);	No reference or explanation provided for hydrolysis half-life value of "stable." All other endpoints estimated from EPI

[218] Appendix C lists six physical and chemical properties. Five of these are included in Table 2-1 (p. 14). The sixth, solubility in n-octanol, is included in text on page 14. The text indicates that the solubility in n-octanol is 0.07 mg/mL whereas Appendix C indicates this value as < 0.07 mg/mL. This discrepancy must be corrected.

[219] Appendix D lists three environmental fate studies (OECD 301F, OECD 305, and OECD 209). The results from 301F are included in Table 2-4 (p. 22). Results from OECD 305 and OECD 209 are not included in Table 2-4. It is not clear why results from OECD 209 are not included in Table 2-4. OECD 305 data are

		OECD 209 (Activated sludge, respiration inhibition test)	Suite which is inappropriate for dyes.
Ecological hazards (Appendix E1 to E3)	3	OECD 201 (Acute aquatic plant toxicity in Duckweed); OECD 202 (Acute freshwater vertebrate study in zebrafish); OECD 203 (acute fresh water invertebrate study in Dapnhia magna)	The ecological evidence base is limited only to studies in aquatic species, and even then only for acute effects. There are no studies of terrestrial organisms. There are no chronic toxicity studies or long-term ecological studies.
Human health hazards - Acute (Appendix F-1)[220]	3	OECD-401 (acute oral single dose in Sprague-Dawley rat); OECD-403 (acute inhalation in Wistar rat); OECD-402 (acute dermal in Sprague-Dawley rat)	Only one acute study is available for each route of exposure. Outdated OECD guideline study for acute oral toxicity.
Human health hazards – Chronic/Repeated dose (Appendix F-2)	0	n/a	No chronic or repeated-dose studies available to examine potential chronic effects.
Human Health Hazard – Reproductive and Developmental Toxicity (Appendix F-3)	1	OECD-421 (Reproductive/developmental screening via gavage in Wistar rats)	

presumably absent from Table 2-4 because the "result" provided in Appendix D is "no bioaccumulation from the 8-weeks bioaccumulation study" as likely gleaned from a study summary (not the full study). Beneath Table 2-4 EPA indicates it has received full studies for OECD 301F and OECD 209 (p. 22). EPA has not appeared to request the full study for OECD 305 and it should. Table 2-4 includes additional environmental fate values (indirect photodegradation, hydrolysis half-life, soil organic carbon:water partition coefficient) all estimated using EPI SUITE.

[220] Appendix F-1 lists three acute toxicity studies (OECD 401, 402, and 403). OECD 402 and OECD 403 are not included in the list of full study reports in EPA's possession (p. 28). EPA must obtain full study reports on these and any other studies it obtains or seeks. On page 28, EPA also lists two non-guideline acute toxicity studies: intraperitoneal study in rats and inhalation toxicity study in rats. These are not reflected in Appendix F-1 and should be.

Skin Irritation and Sensitization	5	OECD-404 (occlusive skin irritation in 2 Weiber Wiener rabbit studies); OECD-405 (eye irritation in 2 rabbit studies); OECD-429 (Skin sensitization LLNA in Male CBA/Ca mouse)	
Genotoxicity and Cancer studies	2	Salmonella typhimrium; Chinese hamster lung fibroblasts	

The evidence base for Pigment Violet 29 hazards is completely inadequate. In fact, it does not even fulfill the OECD Screening Information Data Set (SIDS)[221]—"the minimum amount of data that is required for making an initial hazard assessment of chemicals."[222] Notably absent from the existing information are a repeated-dose or chronic toxicity study. Indeed, there are no chronic studies of Pigment Violet 29 available for ecological or human receptors. EPA does not speak at all to the complete absence of studies evaluating effects resulting from mammalian repeated-dose or chronic exposure studies.

With respect to the absence of data for chronic ecological hazard, EPA notes:

> No studies were identified that characterized the effects of chronic exposure of C.I. Pigment Violet 29 to aquatic species, or the effects to terrestrial species. As a result of uncertainties inherent in extrapolating between acute and chronic exposure regimes and dissimilar environmental receptors, multiple lines of evidence were considered to evaluate the potential for hazards under chronic aquatic exposure conditions and to terrestrial organisms. (p. 27)

However, there is no further discussion in the problem formulation of how EPA plans to consider potential chronic hazards. And what "multiple lines of evidence" EPA is referring to is entirely unclear.

Astoundingly, EPA concludes: "A preliminary review of these study summaries indicates that C.I. Pigment Violet 29 presents a low hazard to human health and environmental receptors." (p. 8) Given the dearth of available information, EPA has certainly not established the low hazard potential of Pigment Violet 29 for ecological or human receptors.

[221] Organisation for Economic Co-operation and Development, Manual for the Assessment of Chemicals, Chp. 2 Data Gathering (Mar. 2012), http://www.oecd.org/chemicalsafety/testing/49944183.pdf.
[222] CHAPTER 2. DATA GATHERING AND TESTING: SIDS, THE SIDS PLAN AND THE SIDS DOSSIER, http://www.oecd.org/chemicalsafety/risk-assessment/chapter2datagatheringandtestingsidsthesidsplanandthesidsdossier.htm (last visited Aug. 14, 2018).

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Additionally, with the exception of hydrolysis half-life and biodegradation, all environmental fate endpoints—also required under OECD SIDS—are estimated using EPI Suite, which EPA itself warns is questionable for dyes. Specifically, footnote b in Table 2-4 notes with respect to estimated EPI Suite data: "There are limited pigment data in the EPI Suite training set, therefore values should be used with caution." (p. 22) With respect to hydrolysis half-life, Table 2-4 simply indicates "stable" with no reference or explanation provided. EPA has not established that it is considering the best science available by relying on modeling based on an admittedly limited data set and failing to obtain additional testing information that is reasonably available.

EPA must immediately use its section 4 and 8 information authorities to fill the significant information gaps associated with Pigment Violet 29.

B. Despite obvious information gaps, EPA shockingly chooses to exclude information on analogs from its review.

In describing existing human health studies available on Pigment Violet 29, EPA notes, "Additional study summaries were identified in the ECHA database, but these were found to be conducted on analogous chemicals, so these studies were not requested at this time." (p. 28) EPA's decision to ignore such studies is both irrational and contradictory. Given the extremely limited evidence base for Pigment Violet 29, EPA should have at least sought out already available and potentially relevant information on analogs. Notably, EPA routinely uses data from analogs to review new and existing chemicals.[223] Indeed, EPA references information associated with analogs in the other sections of the problem formulation. For example, EPA references information on an analog, perylene, in a discussion of potential carcinogenicity (p. 29). The agency's decision to exclude information on analogs for Pigment Violet 29 contradicts standard EPA practice and lacks justification, especially for such a data-poor chemical.

Coupled with its lack of any intent to use its TSCA information authorities to fill gaps, EPA is indicating little interest in basing its decisions about this chemical on anything even approaching the best available science. EPA should include relevant information on appropriate analogs in its review of Pigment Violet 29 while simultaneously using its information gathering authorities under TSCA sections 4 and 8.

74. EPA repeatedly cites low exposure potential as a basis for not further analyzing Pigment Violet 29 despite the meager information available on exposure.

EPA states: "Human exposure to C.I. Pigment Violet 29 through occupational (Figure 2-2), consumer (Figure 2-3) or general population (Figure 2-4) activities and uses is possible, but exposures via all routes (oral, dermal, and inhalation) are expected to be low when physical-chemical properties are considered." (p. 24)

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[223] ABOUT USING PREDICTIVE MODELS AND TOOLS TO ASSESS CHEMICALS UNDER TSCA, https://www.epa.gov/tsca-screening-tools/about-using-predictive-models-and-tools-assess-chemicals-under-tsca (last visited Aug. 14, 2018).

Through this single, sweeping statement EPA declares there is no significant exposure to Pigment Violet 29. A deeper review of EPA's support for this statement reveals glaring holes.

A. Occupational exposures during manufacture.

EPA dismisses occupational exposure during manufacture using a series of weak or otherwise problematic arguments discussed below.

EPA states:

> Workers may be exposed via inhalation and dermal routes. However, absorption via inhalation pathways is expected to be low due to low water solubility and dermal absorption is estimated to be negligible for the neat material (because it is a solid of high molecular weight), and poor absorption in solution (based on high molecular weight and low solubility). (p. 24)

This statement ignores entirely the potential for exposure via inhalation to the neat substance, appearing to exclusively focus on inhalation of Pigment Violet 29 in solution. Elsewhere, EPA attempts to address this issue in a discussion of inhalation exposure from industrial and commercial activities and uses:

> Air emissions are typically relevant for volatile and/or dusty materials and since C.I. Pigment Violet 29 is not volatile, the vapor pathway is not relevant.****Also dust handling systems are in place at the manufacturing facility where the dried powder is added or discharged from the equipment and 99.5% of dust is captured in baghouses. The resulting dust and bags are handled as contaminated industrial waste and sent to a licensed waste handler for disposal. Absorption of C.I. Pigment Violet 29 via inhalation is also expected to be negligible based on low water solubility. Inhalation monitoring has shown that exposure was about 0.5 mg/m^3 over a 12-hr work shift (Mott, 2017a). Due to the low potential for inhalation exposure and low potential absorption and low inhalation toxicity, this pathway will not be further analyzed in the risk evaluation. (p. 30)

EPA relies on Pigment Violet 29's low vapor pressure to dismiss one pathway of inhalation exposure (i.e., volatilization) through air emissions. But EPA appears to ignore the concerns raised by Pigment Violet 29's low water solubility. Multiple studies reveal that inhalation of poorly soluble particles can lead to significant health impacts, including chronic pulmonary inflammation, pulmonary fibrosis, and lung

tumors.[224,225,226] EPA's argument that absorption via inhalation is expected to be negligible because of low water solubility is highly problematic and discordant with current scientific understanding.

Unable to rely on physical chemical properties of Pigment Violet 29 to dismiss inhalation exposures to the substance when present as a dusty material, EPA relies on two personal communications about air concentrations and industrial hygiene controls (Mott, 2017a and Mott, 2017b). EPA relies on these personal communications, from one employee of what EPA states is the only U.S. manufacturer of the chemical, to dismiss all concern for occupational exposure. The content of these personal communications is not even publicly available.[227] Nor is there any mention made of the inherent conflict of interest that this personal communicator has in minimizing any concerns over exposure to the chemical his company makes. Yet EPA relies on this sole source to draw sweeping conclusions that all potential workplace exposures are negligible.

EPA is relying entirely on this personal communication (Mott 2017a) as the basis to assume the air concentration of Pigment Violet 29 in manufacturing facilities is 0.5 mg/m^3 and then uses this value to dismiss any concern about occupational exposures to the neat substance via inhalation. It is entirely unclear how this value was derived and whether it represents the best available science. It is worth noting the uncertainty around this value the first time EPA cites it: "The information indicates a workplace air concentration of 0.5 mg/m^3 over a 12-hour shift (Mott, 2017a). *It is not clear if the monitoring result was for C.I. Pigment Violet 29 or for total dust*." (p. 24, emphasis added) (When the same data are cited six pages later in the problem formulation, EPA drops this caveat entirely; see p. 30.)

EPA also relies on Mott, 2017a for a flimsy defense for why oral and dermal exposures are not expected during manufacture of Pigment Violet 29.

With regard to oral exposure EPA states:

> Oral contact is not a relevant pathway for workers manufacturing C.I. Pigment Violet 29 since eating is not allowed in the production and laboratory work areas and proper personal

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[224] Eileen D. Kuempel, et al., *Human and Animal Evidence Supports Lower Occupational Exposure Limits for Poorly-Soluble Respirable Particles*, 58:9 THE ANNALS OF OCCUPATIONAL HYGIENE 1205 (Nov. 2014), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4618468/.

[225] Oberdörster G., *Lung particle overload: implications for occupational exposures to particles*, 21:1 REGULATORY TOXICOLOGY & PHARMACOLOGY 123 (Feb. 1995), https://www.ncbi.nlm.nih.gov/pubmed/7784625.

[226] Mike Jayjock, *Inhaled Insoluble Particles are more than a Nuisance*, HUMAN HEALTH RISK ASSESSMENT TO CHEMICALS (June 22, 2014), http://jayjock-associates.blogspot.com/2014/06/inhaled-insoluble-particles-are-more.html.

[227] EDF's search of the Pigment Violet 29 problem formulation docket for Mott 2017a and Mott 2017b yielded nothing; the only related item is a document noting that a February 13, 2017 meeting was held between EPA and representatives of BASF, SOCMA, GL+PC, Avanti, CPMA, and Sun Chemical (Robert Mott). Stakeholder Meeting with CPMA – February 13, 2017, https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0725-0026.

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protective equipment (PPE) are expected to be worn at the sole C.I. Pigment Violet 29 US manufacturing facility (Mott, 2017a)." (p. 25)

This assumes oral exposure would only occur if workers eat contaminated food, as well as 100% compliance with the no-eating policy. No information is provided on the type of PPE used and whether it could be sufficiently protective; EPA simply asserts that the equipment and its use are "proper." EPA needs to more closely assess the potential for oral exposure via pathways beyond ingestion of contaminated food, and perform baseline risk evaluation of Pigment Violet 29 in the absence of PPE. *See* Section 13.

With regard to dermal exposure EPA states: "The domestic manufacturer of C.I. Pigment Violet 29 also indicates that workers in production and laboratory areas at their facility wear long sleeves and gloves to prevent dermal exposure (Mott, 2017a)." Again, EPA must perform baseline risk evaluation of Pigment Violet 29 in the absence of PPE. *See* Section 13.

EPA then repeatedly cites a second personal communication from the same individual. The citation provided for Mott, 2017b is "Mott, RC. (2017b). Personal communication between Dr. Robert C. Mott (Sun Chemical Corporation) and Alie Muneer (EPA) regarding release of PV29 to Cooper River [Personal Communication]." As noted earlier, and as is the case with Mott 2017a, Mott 2017b is not publicly available.

EPA uses Mott 2017b to support its assertion of low occupational exposure potential during manufacture. Specifically, EPA states that "[D]ust handling systems are in place at the manufacturing facility that capture dust in baghouses. The efficiency rate is greater than 99.5% (Mott, 2017b; Sun Chemical, 2017b)." (p. 22) No document corresponding to "Sun Chemical, 2017b" is included in the docket.

It would seem that EPA is relying entirely on non-public personal communications (Mott 2017b, Sun Chemical, 2017b) as the basis to assume a 99.5% efficiency rate of dust handling systems. It is entirely unclear how this value was derived and whether it represents the best available science. And, as with PPE, EPA must also evaluate risks in the absence of dust-handling engineering controls.

EPA also cites Mott, 2017b to support an assertion of limited releases to the environment. (p. 24)

EPA must immediately make public the details of the Mott 2017a, Mott 2017b, and all other personal communications relevant to the problem formulation in the docket. EPA's reliance on these personal communications to assert limited exposure to workers (or occupational bystanders) and the environment is highly questionable given the lack of information provided, the inappropriateness of evaluating risk only assuming universal use and efficacy of industrial hygiene controls, and admitted uncertainty in the exposure values obtained.

EPA has authority to require the very types of information, e.g., workplace and environmental monitoring data, on which it here has instead relied on unverified information from a potentially

conflicted source that it has not made public. There is no basis for EPA not to use such authorities, and without doing so the agency is failing to rely on the best available science.

On this point, EPA repeatedly claims that there is only one domestic manufacturer of Pigment Violet 29 (*e.g.*, pp. 22, 24, 25). But EPA acknowledges that it is aware of at least one importer of Pigment Violent 29 importing the chemical below the Chemical Data Reporting (CDR) threshold (p.18) and that there could be additional manufacturers or importers operating below the CDR threshold. Using its authorities under TSCA § 8, EPA could obtain a more definitive and complete understanding of whether and where this chemical is manufactured (including imported) in the United States. This information is reasonably available information, and EPA should use its authorities to obtain it.

B. Occupational exposures to downstream processors and users.

With regard to occupational exposures to downstream processors and users under Section 2.3.5.1 EPA states:

> For downstream processors and users, worker exposure via inhalation through particulates that deposit in the upper respiratory tract or oral routes such as incidental ingestion of C.I. Pigment Violet 29 residue on hands is possible. These exposures are possible during handling solids and spray application of coatings containing C.I. Pigment Violet 29. However, oral and inhalation exposures to downstream processors and users are likely to be limited due to the use of PPEs and negligible oral absorption due to low water solubility [(BASF, 2017), (Sun Chemical, 2017d), (CPMA, 2017a)].
>
> EPA reviewed available Safety Data Sheets (SDSs) for C.I. Pigment Violet 29. The SDSs recommend the use of personal protective equipment to minimize exposure, including the use of chemical-resistant protective gloves and safety glasses with side-shields or a face shield if a splashing hazard exists. It also recommends adequate ventilation when handling C.I. Pigment Violet 29 [(BASF, 2017), (Sun Chemical, 2017d), (Sun Chemical, 2017c)]. (p. 25)

This is incredibly weak evidence on which to base an assertion of limited occupational exposure to downstream processors and users. Basically, EPA has assumed PPE is universally used because companies have told EPA it is or recommend it in their SDSs, and EPA then concludes that oral and inhalation exposures are negligible without any data or analysis as to the actual extent of use, the efficacy, etc., of the PPE. There is absolutely no indication that EPA knows even what type of PPE is being used across various downstream users, nor the extent to which PPE is being consistently and appropriately used. More broadly, as discussed above for manufacturing workers, exposures and risks must also be evaluated in the absence of PPE.

C. Consumer exposures.

With regard to consumer exposures to Pigment Violet 29, EPA states:

> Consumer exposures via oral and dermal routes are expected to be limited based on physical-chemical properties of C.I. Pigment Violet 29. Oral ingestion is expected to be negligible due to the low water solubility (see Table 2-1; 0.01 mg/L) and dermal absorption is estimated to be negligible for the neat material (because it is a solid of high molecular weight) and poor absorption in liquid (based on high molecular weight and low solubility). (p.25)

EPA fails to substantiate its assertion that "consumer exposures associated with identified consumer uses are expected to be limited." Further, EPA's use of Pigment Violet 29's physical chemical properties to assert limited dermal permeation is not supported. A *in silico* model designed to predict the skin sensitization of chemicals, CADRE-SS, [228] indicates that Pigment Violet 29 is at the threshold between a moderate and low skin permeation rate. Additionally, there are examples of dermal permeation by chemicals with greater molecular weights than that of Pigment Violet 29.[229] This evidence indicates that dermal permeation may be higher than EPA suggests for Pigment Violet 29, and that EPA inappropriately relies on molecular weight to assert low skin permeability.

As a general matter, skin permeability cannot be used as an indicator of skin sensitization. There is no direct relationship between skin sensitization and permeability; it is possible for chemicals with low dermal permeability to be skin sensitizers.[230]

Appendix F-4 lists a single skin sensitization study for Pigment Violet 29 with a result simply of "negative." EPA must gather additional information on both dermal permeation and skin sensitization for Pigment Violet 29.

75. EPA must provide access to full studies and other relevant information it has obtained.

EPA indicates that it "has reviewed the robust study summaries of physical/chemical properties, environmental fate, human health hazard and environmental hazard studies in these databases, (summarized in Appendix C- Appendix F) and obtained the full study reports from the data owners for in-depth review." (p. 8) In conformance with TSCA section 14(b)(2), EPA must promptly make these full health and safety studies publicly available immediately. For Pigment Violet 29 this includes the full studies obtained from the ECHA database and the full studies from the FDA Food Additives Petition (FAP) 8B4626 submitted by BASF. These studies do not appear to be included in the EPA dockets associated with Pigment Violet 29.

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[228] Jakub Kostal & Adelina Voutchkova-Kostal, *CADRE-SS, an* in Silico *Tool for Predicting Skin Sensitization Potential Based on Modeling of Molecular Interactions*, 29:1 CHEMICAL RESEARCH IN TOXICOLOGY 58 (Jan. 2016), https://www.ncbi.nlm.nih.gov/pubmed/26650775

[229] Taravat Ghafourian & Shadi Fooladi, *The effect of structural QSAR parameters on skin penetration*, 217:1-2 INTERNATIONAL JOURNAL OF PHARMACEUTICS 1 (Apr. 2001), https://www.ncbi.nlm.nih.gov/pubmed/11292537

[230] Vinicius M. Alves, et al., *Predicting chemically-induced skin reactions. Part II: QSAR models of skin permeability and the relationships between skin permeability and skin sensitization*, 284:2 TOXICOLOGY AND APPLIED PHARMACOLOGY 273 (Apr. 2015), https://www.ncbi.nlm.nih.gov/pubmed/11292537

As a general matter, EPA should obtain and make public full studies of any robust summaries it obtains on chemicals undergoing risk evaluation. It is not sufficient that EPA rely on or provide to the public only robust study summaries.

More broadly, EPA has relied on a substantial amount of industry-provided information, much of which is not publicly available—for example, personal communications, information submitted as part of a food additives petition, and information related to conditions of use apparently gathered during a September 15, 2017, meeting "with several representatives from trade associations." (p. 15) EPA must make all information pertaining to Pigment Violet 29 publicly available in the docket.

76. Environmental release information is insufficient or absent.

EPA repeatedly cites non-public personal communications or EPI Suite-modeled environmental fate information as its basis for ruling out significant environmental release. These sources are of questionable reliability.

EPA again relies on Mott, 2017b for information regarding yield loss during manufacturer (p. 22), dust handling systems efficiency rates (p. 22), and transfer of lost yield to an on-site aboveground biological wastewater treatment system (p. 23) As discussed in Section 74.A, Mott, 2017b is a personal communication that EPA has not made publicly available. Its reliability, and the extent to which it reflects the best available science, is entirely uncertain.

With regard to releases from downstream processors, EPA indicates the following:

> No data pertaining to environmental releases from the twenty downstream industrial facilities that process C.I. Pigment Violet 29 into plastics, paints and coatings were identified. These uses account for 10% of the total production volume. However, CPMA indicated that all of these facilities are subject to EPA and state regulations resulting in limiting releases to air, water, and land of materials to the environment.
>
> Exposure and releases are possible when handling concentrated C.I. Pigment Violet 29 but once it is encapsulated in plastics or paint resins, it is not expected to leach out [21 CFR 178.3297, (BASF, 1998a)]. (p. 23)
>
> AND
>
> As outlined above, physical-chemical and fate properties as well as engineering controls limiting manufacturing (the largest use) releases are expected to result in limited exposure to water and sediment, groundwater via biosolids, landfill leaching, and air. It is estimated that less than one pound per day of C.I. Pigment Violet 29 is being released as the overall total of the National Pollutant Discharge Elimination System (NPDES)-permitted total suspended solids (TSS) discharges from the sole US manufacturer (Mott, 2017b). Because volumes used by downstream users are markedly less than the manufacturer (less than 5% each), it is expected that there will be minimal releases to water and sediment, groundwater via biosolids, landfill leaching, and air.

Where releases do occur, they are expected to result in limited environmental exposures. Specifically, releases of C.I. Pigment Violet 29 to water and sediment could occur during the wastewater treatment process following manufacturing/processing through possible releases of TSS, but these releases and corresponding aquatic exposures are expected to be limited since the high sorption of this chemical to organic matter (Log Koc = 5.0; see Table 2-4) will result in the vast majority of C.I. Pigment Violet 29 being captured as sludge in wastewater treatment facilities which is subsequently disposed of via incineration or landfill disposal. Similarly, the strong sorption properties would be expected to limit exposure via migration to groundwater from C.I. Pigment Violet 29 disposed of in landfills or applied via biosolids. (p. 24)

AND

Although the persistence and tendency to sorb to sediment means that there is the potential for entry into the aquatic food web, available data indicate that the BAF is low so uptake and bioaccumulation is likely to be limited. (p. 23-24)

These excerpts raise a number of concerns:

- EPA readily admits that is has no information on potential releases from downstream users. Instead EPA simply indicates that "CPMA [an industry trade association] indicated that all of these [downstream] facilities are subject to EPA and state regulations resulting in limiting releases to air, water, and land of materials to the environment." (p. 23) EPA doesn't even suggest that it has evaluated whether CPMA's statement is true and further, if so, the extent to which these EPA and state regulations are actually effective in limiting release.
- In a single sentence, EPA indicates that release of Pigment Violet 29 is possible from downstream users and then pivots to the expectation that the substance will not leach out of plastics or paint resins. For neither of these two distinct issues, however, has EPA addressed the need to obtain actual information on release potential during processing.
- EPA relies on Mott, 2017b for its only estimate of release of Pigment Violet 29 though surface discharge. As discussed in Section 74.A, this is a personal communication that is not publicly available and is of questionable reliability.
- EPA relies on environmental fate information (Log Koc) to dismiss aquatic exposures even though, as discussed in Section 73.A, EPA itself indicates that values derived from EPI Suite for dye chemicals should be used with caution. In fact the only environmental fate endpoint derived with measured data is biodegradability; the result of which indicates that Pigment Violet 29 is highly persistent. It is also worth noting that on pages 23-24 EPA indicates that it "did not find any environmental monitoring data (e.g., presence in air, soil, sediment, surface water, or biota)***[nor] biomonitoring data for C.I. Pigment Violet 29 (U.S. EPA, 2017a)." Absence of data does not support a finding of absence of the presence of the chemical in the environment or people.
- EPA relies on environmental fate data (BAF) to support an assertion that entry of Pigment Violet 29 into the aquatic food web will be limited. However, again, EPA is using a BAF derived from EPI Suite that is not reliable for Pigment Violet 29.

77. EPA's review of a residual, naphthalimide, is entirely inadequate and raises major red flags for EPA's treatment of residuals, by-products, and degradation products in future risk evaluations.

In the problem formulation, EPA identifies naphthalimide as a residual of C.I. Pigment Violet 29 as manufactured. The totality of the agency's brief discussion is as follows:

> There are no known by-products or degradation products resulting from the manufacture of C.I. Pigment Violet 29. There is a residual amount of naphthalimide, the starting material used in the fusion, at approximately 1% (Sun Chemical, 2017a). Per robust study summary reports from the ECHA Database, the hazard profile of naphthalimide is low for human health and environmental receptors (ECHA, 2017a). Based on the minimal amount of naphthalimide released from manufacturing and low hazard, EPA will not conduct any further analysis of the naphthalimide residual associated with C.I. Pigment Violet 29 production. (p. 14)

This is an entirely inadequate review of the potential risks associated with naphthalimide, based solely on industry information provided to and not evaluated by ECHA. (See Section 8.B) It certainly does not represent use of best available science. EPA must conduct a much more extensive review of the extent of presence and the potential risks of naphthalimide before reaching a decision to do no further analysis.

The implications of EPA's dismissal of any need to evaluate the naphthalimide residual are significant. EPA has indicated elsewhere that it will not analyze exposures and risks of chemicals only present incidentally (e.g., as an impurity or byproduct) (e.g., see 1,4-dioxane problem formulation at 18) when preparing risk evaluations, suggesting that the appropriate time for such evaluation may be when the parent substance is undergoing risk evaluation.[231] EDF strongly disagrees that EPA can disregard a chemical's presence as an impurity or byproduct when evaluating the chemical, and our concerns are only affirmed and increased by EPA's cursory dismissal of the naphthalimide residual associated with Pigment Violet 29.

78. EPA's discussion of waste handling, treatment and disposal is lacking.

With regard to waste handling, treatment and disposal EPA states:

> Releases of C.I. Pigment Violet 29 from recycling of used papers and plastic articles containing C.I. Pigment Violet 29 is possible. However, due to its low water solubility and high sorption to particulates and biosolids, most C.I. Pigment Violet 29 in aqueous waste streams is expected to be captured in the waste water treatment systems. As a result of the lack of exposure expected to result from this pathway, EPA plans no further analysis of this pathway for workers or occupational non-users in the risk evaluation. Figure 2-3 in the C.I. Pigment Violet 29 Scope Document presented the possible

[231] Problem Formulation of the Risk Evaluation for 1,4-Dioxane at 18, *available at* https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0723-0064.

> exposure pathways, exposure routes and hazards to human receptors from consumer activities and uses of C.I. Pigment Violet 29 (U.S. EPA, 2017c). Due to these releases, pathways and routes of exposure, EPA has concluded no further analysis of these pathways is warranted, as indicated in Figure 2-3. (p. 31)

EPA has not provided any actual evidence that Pigment Violet 29 will be captured in wastewater treatment systems. Information related to wastewater treatment included in the problem formulation appears to be primarily, if not exclusively, from the Mott, 2017b personal communication reference (see for example section 2.3.4 on page 24 and section 2.5.2.2 on page 33). Moreover, the high sorption to particles and biosolids is based on EPI Suite data that is not reliable for Pigment Violet 29.

79. EPA heavily relies on information received by ECHA and FDA to assert low exposure and hazard potential, yet it has not reviewed the corresponding full studies it has apparently has received and they are not publicly available.

EPA states:

> The analysis plan for C.I. Pigment Violet 29 therefore consists of evaluating the study reports received by the Agency to ensure that the studies are scientifically sound and the results are consistent with EPA's preliminary review of the robust summaries in the ECHA database and the FDA Food Additive Petition (FAP) 8B4626 for C.I. Pigment Violet 29 (BASF, 1998a). If the review of these study reports indicates that the results are not scientifically sound or consistent with the robust summary reports, EPA may conduct additional analysis in developing the Draft Risk Evaluation for C.I. Pigment Violet 29, which may include changes to the pathways analyzed. (p. 8)

Remarkably, EPA relies heavily on robust summaries received by ECHA and FDA from industry to conclude in the problem formulation that EPA will not further analyze any Pigment Violet 29 condition of use without even yet having reviewed the corresponding full studies EPA apparently has obtained—studies that are not publicly available. Instead, EPA indicates that it plans to review the full studies, at some point after publishing the problem formulation, to ascertain whether the robust summaries are reliable and consistent with the full studies. If concerns arise, EPA indicates that it "may conduct additional analysis." EPA seems to be indicating that it may also choose to do nothing at all.

The premature decision not to further analyze any condition of use is nothing less than shocking, as is EPA's indication that it may still do nothing even if the full studies call into question the robust study summaries EPA has relied on to develop the problem formulation, and on which it bases its premature decision. These decisions do not reflect a best available science approach to conducting risk evaluations.

* * * * *

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

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October 30, 2018

Andrew Wheeler
Acting Administrator
U.S. Environmental Protection Agency
Mail code: 1101A
1200 Pennsylvania Avenue, NW
Washington, D.C. 20460

Re: *Public Comment and Peer Review Process for Initial 10 Risk Evaluations under TSCA*

Dear Acting Administrator Wheeler:

Our organizations are committed to assuring the safety of chemicals used in our homes, workplaces and in the many products to which our families and children are exposed each day. During the legislative process to amend the Toxic Substances Control Act (TSCA), we worked hard to maximize public health protection and to assure that EPA has the necessary authority to evaluate and eliminate the risks of unsafe chemicals. We strongly support a proactive approach to implementing the new law that uses the improved tools that Congress gave EPA to deliver significant health and environmental benefits to the American public.

An early test of TSCA implementation is the initial group of 10 risk evaluations that EPA is conducting under section 6(b)(2)(A). The chemicals subject to these evaluations raise significant health and environmental concerns and have widespread exposure. The available hazard and exposure data on these chemicals are extensive and present numerous important scientific issues. The risk evaluations will fall short under TSCA and seriously damage EPA's credibility if they are not based on the best available science.

We understand that EPA is planning to release draft evaluations in late 2018 and early 2019 and then will seek public comment and peer review with the goal of finalizing the evaluations by the end of 2019. If EPA cuts corners on public comment and peer review, the quality of the evaluations will be fatally compromised. Thus, TSCA requires EPA to design a process which assures that the final evaluations fully reflect the input of stakeholders and leading independent experts, are based on the weight of the scientific evidence and the best available science, and draw on all reasonably available data and information.

Extensive guidance on the minimum elements of peer review for important and influential scientific work products is provided in OMB's Peer Review Bulletin and EPA's Peer Review Handbook. The application of this guidance is reflected in the public comment and peer review processes used for EPA's Work Plan risk assessments under the old law and recent IRIS assessments. Based on this roadmap, we recommend that EPA incorporate the following minimum steps in its public comment and peer review process for the 10 risk evaluations:

- EPA should allow 120 days for comments on the draft evaluations
- Some evaluations (e.g. for solvents) should be grouped together for review by a single panel while substances that raise unique issues (e.g. asbestos) should be reviewed separately
- Separate review panels should also be established to address EPA's systematic review methodology and other cross-cutting science issues
- Scientists under consideration as peer reviewers – including all members of the Scientific Advisory Committee on Chemicals (SACC) -- should undergo a rigorous review for conflicts of interest and bias regarding the 10 chemicals, including full disclosure to EPA of all sources of funding and business and

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financial relationships, and the public should have an opportunity to comment on all candidate reviewers

- EPA should seek public comment on the draft charges for the peer reviews of the 10 evaluations
- The public should have the opportunity to provide written and oral statements to peer review panels
- The panels should prepare reports which summarize the recommendations of panel members and common themes in their reviews, fully document areas of agreement and disagreement and capture the views of panel members with common areas of expertise
- EPA should seek the advice of its children's health protection advisory committee on the 10 evaluations
- EPA's final risk evaluations should respond to all public comments and peer review recommendations

Section 6(b)(4)(G) of TSCA gives EPA up to three years to complete a risk evaluation but allows this deadline to be extended for an additional 6 months. While EPA should in general try to meet the three year deadline, an extension of six months for the initial 10 risk evaluations would provide critical breathing space for the public comment and peer review process. An additional 6 months would increase the likelihood that EPA receives high-quality comments, allow the reviewers the time necessary for an in-depth examination of each draft evaluation and preparation of a detailed report, and enable EPA staff to fully digest this feedback and incorporate it in the final evaluations. It would be a serious mistake for EPA to cut corners on these steps and to rush final evaluations out the door without the thoughtful comments and expert advice necessary to assure that EPA uses the best available science and all reasonably available information in assessing chemical risks.

1. EPA Should Allow 120 Days for Comments on the Draft Evaluations

For each of the 10 chemicals, the draft evaluations will address multiple health and ecological end-points, combine hazard information with exposure analysis, and determine the risks presented by numerous conditions of use. Thus, they will be more comprehensive and complex than the Work Plan risk assessments conducted under the old law, which focused on a limited set of end-points and uses. The evaluations will also have far-reaching regulatory consequences because they will be used to determine whether the 10 chemicals present an unreasonable risk of injury and should be restricted under section 6(a) of TSCA.

The breadth, novelty and complexity of the 10 risk evaluations will place heavy demands on commenters. As a result, preparing meaningful and thorough comments will require a significant investment of time and resources by our organizations and leading experts in the scientific community. These challenges will be greatly magnified by the likelihood that the comment periods for the 10 evaluations will overlap, requiring stakeholders and experts to review and prepare comments on numerous evaluations simultaneously.

Comment periods for Work Plan risk assessments and recent IRIS assessments have varied from chemical to chemical. Some were 60 days, others were 90 days, and one (for methylene chloride and N-methylpyrollidone) was nearly five months. We believe EPA should allow at least 120 days for comments on the TSCA risk evaluations based on their scope and complexity, the large amount of data and analysis they will contain, their regulatory and policy implications, and the uniquely heavy resource demands of addressing multiple chemicals simultaneously. [1]

[1] EPA's final risk evaluation rule (40 CFR 702.49(a)) provides that EPA will provide "no less than a 60-day comment period" for draft evaluations. Obviously, the rule contemplates longer comment periods in appropriate cases.

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2. Under the SACC Umbrella, Chemicals Raising Common Issues Should be Reviewed by a Single Panel While Chemicals with Unique Issues Should be Reviewed Separately

Under OMB's 2005 Final Information Quality Bulletin for Peer Review, the TSCA risk evaluations qualify as Highly Influential Scientific Assessments (HISAs) because they not only will have "a clear and substantial impact on important public policies" but will be "novel, controversial, or precedent-setting or ha[ve] significant interagency interest."[2] OMB requires a robust independent peer review process for such assessments, noting that that the "intensity of peer review should be commensurate with the significance of the information being disseminated and the likely implications for policy decisions" and that "the need for rigorous peer review is greater when the information contains precedent-setting methods or models, presents conclusions that are likely to change prevailing practices, or is likely to affect policy decisions that have a significant impact."[3]

EPA's Peer Review Handbook uses the same definition of HISAs, emphasizing that "[t]he more far-reaching or significant the impacts of a scientific assessment, the more appropriate it is to categorize the product as an HISA." The Handbook advises that HISAs "are expected to undergo rigorous external peer review with opportunities for public participation."[4]

The Science Advisory Committee on Chemicals (SACC), created by the new law to provide expert advice to the TSCA program, is an appropriate umbrella body to oversee peer review of the 10 risk evaluations. We recommend that EPA utilize the scientific expertise of SACC efficiently while assuring that unique chemical-specific issues receive the special consideration they deserve. Thus, risk evaluations on solvents with similar uses and chemical compositions (trichloroethylene, methylene chloride, perchloroethylene and carbon tetrachloride) should be grouped together and reviewed by a single panel. However, other risk evaluations (for example, on asbestos and the HBCD cluster) will require separate panels because they raise unique issues that call for specific types of expertise. [5]

Even where risk evaluations are grouped together, it will be essential to develop chemical-specific charge questions, augment the review panel with experts knowledgeable about particular chemicals and their data-sets, and issue separate reports on each risk evaluation. Meetings of the panel should also be structured to assure adequate opportunity for public comment on each risk evaluation. This would assure that each evaluation receives the full attention of the review panel and can be examined in sufficient depth to provide thoughtful and considered feedback to EPA.

3. Separate Review Panels Should be Established for Systematic Review and other Cross-Cutting Science Issues

Separate review panels should be established to address cross-cutting science issues presented by all 10 evaluations. The most important of these issues is the "systematic review" criteria EPA is using to determine

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[2] 70 Federal Register 2664, 2671 (January 14, 2005).
[3] Id at 2668.
[4] U.S. Environmental Protection Science and Technology Council. Agency Peer Review Handbook 4th Edition; October 2015, at 43, 55, available at https://www.epa.gov/osa/peer-review-handbook-4th-edition-2015
[5] While EPA's September 13, 2018 Federal Register notice seeks nominations of experts to assist in reviewing the 10 evaluations, it makes no effort to identify the specific areas of expertise relevant to individual chemicals. 83 FR 46487. This makes it difficult for the public to choose which experts to nominate and runs the risk that EPA will lack the ability to select panel members qualified to address the unique issues raised by individual evaluations.

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the quality of individual studies and determine how much weight they should receive in the evaluations.[6] These criteria are out of step with other systematic review approaches used within EPA and across the government and were not peer reviewed before they were applied to the 10 chemicals. We have urged EPA to replace its criteria with another systematic review methodology that has been peer reviewed and reflects mainstream scientific thinking. If EPA continues to reject this course, it must at a minimum assure that its systematic review criteria receive careful, independent scrutiny by a group of experts knowledgeable about the design and application of systematic review methods. Given the novelty and importance of EPA's approach to systematic review, finalizing the 10 risk evaluations without such scrutiny would violate EPA's Peer Review Handbook and TSCA's requirement to use the best available science.

Other cross-cutting methodologies used to determine the weight of the evidence or for data integration and interpretation should likewise receive independent expert review. Examples include the use of mechanistic data and thresholds for cancer and non-cancer effects.

4. Candidates for Each Panel Should Undergo a Rigorous Conflict of Interest Review Which Includes Input from the Public

The SACC must comply with the mandate of the Federal Advisory Committee Act (FACA) that it be "fairly balanced in terms of the points of view represented and the functions to be performed" and protected from "inappropriate[] influence[] by the appointing authority or by any special interest." 5 U.S.C. app. 2 § 5(b)(2)-(3).

Consistent with FACA, the OMB Handbook underscores the importance of assuring that external peer reviewers lack conflicts of interest and are impartial:

> The National Academy of Sciences defines ''conflict of interest'' as any financial or other interest that conflicts with the service of an individual on the review panel because it could impair the individual's objectivity or could create an unfair competitive advantage for a person or organization. This standard provides a useful benchmark for agencies to consider in selecting peer reviewers. Agencies shall make a special effort to examine prospective reviewers' potential financial conflicts, including significant investments, consulting arrangements, employer affiliations and grants/contracts. Financial ties of potential reviewers to regulated entities (e.g., businesses), other stakeholders, and regulatory agencies shall be scrutinized when the information being reviewed is likely to be relevant to regulatory policy. The inquiry into potential conflicts goes beyond financial investments and business relationships and includes work as an expert witness, consulting arrangements, honoraria and sources of grants and contracts

70 Fed. Reg. 2670.

While SACC members may have been screened for conflicts of interest (COIs) when they were initially selected, this review likely did not focus directly on the 10 chemicals undergoing risk evaluations or on broader scientific issues raised by these evaluations. Under applicable guidelines, financial ties to manufacturers of one of the 10 chemicals or consulting work or research for industry on these chemicals or the broader scientific issues they raise would present COI and impartiality concerns that may be disqualifying. To assure that these issues are fully addressed, a further examination of potential conflicts must be

[6] 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

conducted before SACC members are cleared to serve as peer reviewers of the 10 evaluations. Any new experts added to SACC or selected for individual panels must likewise be screened for conflicts of interest.

Standard EPA practice for major peer reviews is to seek public comment on the qualifications of candidate reviewers, including whether they should be barred from serving because of conflicts of interest or bias. EPA accomplishes this by publishing a notice identifying candidate reviewers and soliciting public input. For example, EPA recently issued a call for public comment on candidates for its Science Advisory Board (SAB). EPA should follow this process for the 10 risk evaluations and include both current SACC members and additional experts under consideration for SACC membership or ad hoc participation in specific panels.

5. EPA Should Seek Public Comment on the Draft Peer Review Charge for Each Risk Evaluation

According to EPA's Peer Review Handbook, a "charge is a set of focused questions that identifies the scientific and technical issues on which the Agency would like feedback and invites suggestions for improving the document as a whole. . . . Preparing a good charge is time well-spent, as the charge is crucial for an effective peer review." Handbook, at 82.

Public input is often invaluable in shaping the charge and the EPA SAB and individual EPA offices normally seek comments on draft charge questions before finalizing them. Because the TSCA risk evaluations are unprecedented, framing the right set of charge questions will be particularly important to assure meaningful peer review. Interested parties should therefore have the opportunity to weigh in on what questions the charge should include. Significantly, EPA's "framework rule" for TSCA risk evaluations emphasizes that "EPA plans to take public comment on the charge questions given to peer reviewers." 82 Fed. Reg. 33744.

6. The Public Should Have the Opportunity to Provide Written and Oral Statements to the Peer Review Panels

The EPA Peer Review Handbook recommends "that the process [for HISAs] should include a public meeting, whenever feasible and appropriate, . . . [at which] interested members of the public can make oral presentations on scientific issues." Handbook, at 86. For the TSCA Work Plan assessments, the Agency convened public peer review meetings and allowed interested parties to provide written comments and oral statements to the reviewers. The SAB implements a similar public participation process for its review of IRIS assessments. The Handbook recommends separating the initial public comment period from the later submission of written materials to the panel – an approach that EPA followed for the Work Plan assessments and uses for IRIS reviews.

This model should be followed for the 10 risk evaluations. In addition to allowing submission of written comments to the reviewers, EPA should schedule sufficient public meeting time to accommodate oral statements by all interested parties who wish to share their views and afford the panel members ample opportunity to discuss the scientific issues among themselves so they can provide meaningful feedback to the Agency.

7. The Panels Should Prepare Informative Reports That Summarize Major Recommendations and Document the Range of Views among Panel Members

Peer review reports are most useful to the Agency and public when they are the outgrowth of dialogue among panel members and, as a result, distill key panel recommendations and capture common themes, areas of agreement and disagreement, and the views of panel members with shared areas of expertise. The SAB follows this model and, to that end, circulates draft reports to panel members for review and comment

and convenes group drafting sessions. This interaction among panel maximizes the likelihood that the Agency receives coherent and thoughtful feedback while ensuring that panel members are able to express and record divergent views. By contrast, where panel members submit their individual responses to charge questions with no give-and-take and group discussion, the resulting report is often a collection of unsynthesized opinions that are difficult for Agency scientists to process and less useful in improving EPA's work product.

For the precedent-setting risk evaluations underway under TSCA, we strongly urge EPA to assure that peer review panels have sufficient time for internal dialogue and to develop reports that are thoughtful and thorough, coherently address all the issues, summarize key panel recommendations and fully present panel member views, including both majority and dissenting views. Final peer review reports should be immediately made available to the public.

8. EPA Should Seek the Advice of its Children's Health Protection Advisory Committee on the 10 Evaluations

Children are explicitly identified as a "potentially exposed or susceptible population" in section 3(12) of TSCA and EPA risk evaluations must specifically address whether a substance presents an unreasonable risk of injury to such populations under section 6(b)(4)(A). EPA's Children's Health Protection Advisory Committee (CHPAC) is a body of external researchers, academicians, health care providers, environmentalists, state and tribal government employees, and members of the public with expertise on children's health issues. It is the preferred source of advice within the Agency on regulations, research, and communications related to children's health. Its input will be vital given the central role of children's health protection in TSCA risk evaluations. EPA should explicitly request the CHPAC's review of the 10 risk evaluations and ask for its views in writing.

9. EPA's Final Risk Evaluations Should Respond to All Public Comments and Peer Review Recommendations

The final stage of the peer review process is the Agency's response to the panel's recommendations and revisions to its scientific work product to reflect the panel's feedback. This part of the process must be fully transparent. As explained in the EPA Handbook:

> The credibility of the final influential work product is likely to be enhanced if the public understands how the Agency addressed the specific concerns raised by the peer reviewers. Therefore, for HISAs, EPA offices should prepare a written response to comments in the peer review report explaining (1) the Agency's agreement or disagreement with the views expressed in the report; (2) the actions that have been or will be taken to respond to the report; and (3) the reasons that the EPA office believes those actions satisfy any key concerns or recommendations in the report. Any responses also should be posted in the SI website database.

Handbook, at 87. EPA should fully implement these steps when finalizing its 10 risk evaluations.

10. EPA Should Extend the Deadline for Completing the Evaluations by Six Months

Section 6(b)(4)(G) of TSCA gives EPA up to three years to complete a risk evaluation but allows this deadline to be extended for an additional 6 months. EPA should take advantage of this provision and extend the completion date for the first 10 risk evaluations until June 30, 2020.

This extension would provide additional breathing space for the public comment and peer review process, increasing the likelihood that EPA receives high-quality comments and giving the reviewers the time

necessary for an in-depth examination of draft evaluations and preparation of detailed reports. It would also give EPA scientists more time to consider the public comments and peer review reports, revise the draft evaluations to incorporate this input and develop a detailed response to the recommendations of the commenters and review panels.

For the four Work Plan assessments completed under the old law, the average amount of time from the start of the public comment period to publication of the final assessment was 19 months. Comparable stages in the IRIS process have been even more protracted, averaging 3 years for recent assessments. The TSCA risk evaluations will be more complex than the Work Plan assessments and the public comment and peer review process will therefore require greater time and effort. It would be a serious mistake for EPA to cut corners on these steps and to rush final evaluations out the door before EPA scientists have carefully considered the expert advice they receive. EPA should thus take the additional six months provided by law to complete the evaluations.

In sum, we believe the above recommendation for the public comment and peer review process for the 10 evaluations are necessary to meet the requirements of TSCA and assure credible, science-based judgments about chemical risks and urge EPA to adopt them. We look forward to discussing the details of the upcoming process with your staff.

Please contact SCHF counsel Bob Sussman with any questions at bobsussman1@comcast.net.

Respectfully submitted,

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August 16, 2018

Ms. Christina Motilall
Risk Assessment Division
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue NW
Washington, DC 20460

Submitted via the Federal eRulemaking Portal: https://www.regulations.gov/

Re: EPA-HQ-OPPT-2016-0723, EPA-HQ-OPPT-2016-0725, EPA-HQ-OPPT-0732, EPA-HQ-OPPT-2016-0733, EPA-HQ-OPPT-2016-0735, EPA-HQ-OPPT-2016-0736, EPA-HQ-OPPT-0737, EPA-HQ- OPPT-2016-0741, EPA-HQ-OPPT-2016-0742, and EPA-HQ-OPPT-0743

Dear Ms. Motilall,

The American Chemistry Council (ACC) is pleased to submit the attached comments on EPA's problem formulations for risk evaluations to be conducted on the initial 10 chemicals under TSCA.

These comments align with our comments on the proposed Application of Systematic Review in TSCA Risk Evaluations, which have been separately filed and are also attached here as Attachment B. These comments should be considered together.

Please let me know if you have any questions regarding these comments. I can be reached at 202-249-6440 or by email at Suzanne_Hartigan@americanchemistry.com.

Sincerely,

Suzanne Hartigan

Suzanne Hartigan, Ph.D.
Senior Director
Regulatory and Technical Affairs

AMERICAN CHEMISTRY COUNCIL COMMENTS ON THE PROBLEM FORMULATIONS FOR THE U.S. ENVIRONMENTAL PROTECTION AGENCY'S INITIAL 10 CHEMICALS IDENTIFIED FOR RISK EVALUATION

August 2018

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Executive Summary

The American Chemistry Council (ACC)[1] appreciates the opportunity to provide comments on the problem formulations for the initial 10 chemicals to undergo risk evaluation under the amended Toxic Substances Control Act (TSCA). ACC supports EPA's practical and thoughtful approach to reviewing the circumstances of manufacturing, processing, distribution, use, and disposal of these chemicals to inform the development of the scoping process. The problem formulations show the Agency's commitment to identifying and reviewing those conditions of use that represent the greatest potential for risk and document its efforts to gather the best available information to use in the risk evaluations.

ACC remains committed to the efficient and effective implementation of the TSCA amendments and makes several recommendations to the Agency for its consideration in these and future scoping documents for TSCA risk evaluations:

- **Systematic Review:** EPA's development of a structured process to identify, evaluate, and integrate evidence from both the hazard and exposure assessments developed during the TSCA risk evaluations is appropriate and will provide increased transparency into the TSCA risk evaluation process.
- **Conditions of Use**: EPA should develop a framework for its scoping approach that articulates its process for deciding when conditions of use will be in or out of scope of the risk evaluation. This would help streamline EPA's future efforts, increase transparency, and help industry anticipate EPA's information needs in the risk evaluations.
- **Coordination with Other Appropriate Federal Executive Departments or Agencies:** EPA should describe its coordination with other federal agencies—OSHA in particular—to clarify how it will undertake its TSCA Section 9(d) consultation obligations. This coordination is essential to avoid duplicative and unnecessary regulation.
- **Tiered Approaches to Assessment**: EPA should apply tiered approaches throughout the risk evaluation process to enable EPA to meet TSCA's deadlines, adhere to TSCA's science standards, and enable both EPA and the regulated community to apply limited resources efficiently.
- **Road Map and Guidance on Tiered Exposure Assessments**: A road map showing EPA's approach to tiered exposure assessments and related guidance would be useful. Moreover, EPA should be more transparent about the specific exposure models, occupational exposure limits, and margins of exposure it intends to rely upon in its risk

[1] The American Chemistry Council (ACC) represents the leading companies engaged in the business of chemistry. ACC members apply the science of chemistry to make innovative products and services that make people's lives better, healthier and safer. ACC is committed to improved environmental, health and safety performance through Responsible Care®; common sense advocacy designed to address major public policy issues; and health and environmental research and product testing. The business of chemistry is a $768 billion enterprise and a key element of the nation's economy. It is among the largest exporters in the nation, accounting for fourteen percent of all U.S. goods exports. Chemistry companies are among the largest investors in research and development. Safety and security have always been primary concerns of ACC members, and they have intensified their efforts, working closely with government agencies to improve security and to defend against any threat to the nation's critical infrastructure.

evaluations. To ensure consistency across the Agency's exposure assessments, EPA should rely upon standard exposure scenarios.

- **Occupational Exposure**: EPA should offer more detail on the data and information it plans to consider in its occupational exposure assessments. EPA should provide broader guidance on how it will evaluate occupational exposures under TSCA, including consideration of the most up-to-date information.
- **Ecological Exposures:** EPA should explain its tiered approach to ecological exposures and consider further standardization of emission scenarios and environmental release categories, including updating Generic Scenarios used in conjunction with ChemSTEER.
- **Consumer Exposures**: EPA must ensure that its models are publicly available, accessible, and can be readily used by knowledgeable professionals. Further, EPA should provide greater clarity about how it will assess consumer exposure to chemicals in products.
- **Hazard Assessment**: EPA should use integrated hazard assessments for regulatory decision making, and should work to identify, develop, and integrate non-animal methods. EPA should consider mode of action (MOA) in problem formulations and, where appropriate and supported by the data, ACC recommends EPA adopt and apply the World Health Organization (WHO)/International Programme on Chemical Safety (IPCS) MOA framework in risk assessments.
- **Ecological Hazard Assessment**: EPA should identify the higher-tier approaches it may use for determining a hazard threshold, especially for data rich chemicals.

Each of these recommendations is discussed in more detail below.

I. General Considerations

A. EPA Must Use a Structured Process to Identify, Evaluate, and Integrate Hazard and Exposure Information Developed During the TSCA Risk Evaluations.

Section 26 of TSCA mandates that EPA make science-based decisions under Sections 4, 5, and 6 of TSCA in a manner consistent with the best available science and the weight of the scientific evidence.[2] EPA's development of a structured process to identify, evaluate, and integrate evidence from both the hazard and exposure assessments developed during the TSCA risk evaluations is appropriate and will provide increased transparency into the TSCA risk evaluation process. Systematic review approaches applied in many fields provide frameworks to identify, select, evaluate, and integrate scientific evidence to support a conclusion.[3] ACC's comments on EPA's proposed approach, "Application of Systematic Review in TSCA Risk Evaluations,"[4] (Systematic Review) have been filed in that docket. Those comments are also attached here and

[2] 15 U.S.C. §§ 2625(h) and (i).
[3] Wikoff, D.S. and Miller, G.W. 2018. Systematic reviews in toxicology (Editorial). Toxicological Sciences, 163(2): 335-37.
[4] US EPA, Application of Systematic Review in TSCA Risk Evaluations, Office of Chemical Safety and Pollution Prevention, Office of Pollution Prevention and Toxics, EPA Document # 740-P1-8001. Available at https://www.epa.gov/sites/production/files/2018-06/documents/final_application_of_sr_in_tsca_05-31-18.pdf

incorporated by reference to these comments on the problem formulations.[5] In general, EPA should make the results of its systematic review process available as part of the docket for each risk evaluation, including its selection of key studies and study quality evaluations.

B. Scoping Decisions Should Consider Best Available Information and Greatest Potential for Risk.

EPA has identified those conditions of use that will be within the scope of the risk evaluations, as well as those that will be excluded. The risk evaluation rule makes clear that EPA should focus on those conditions of use that raise the greatest potential for risk.[6] ACC generally supports the approach taken to addressing conditions of use within each of the 10 problem formulations. This approach allows EPA to be efficient, while still addressing the highest priority conditions of use that pose the greatest potential risk.

The problem formulation documents present a thoughtful approach to identifying current uses that are appropriate for inclusion within the scope of the risk evaluation. We also appreciate EPA's efforts to explain why the conditions of use that are not within scope will be excluded. ACC encourages continued stakeholder engagement with manufacturers and users of these chemicals throughout the risk evaluation process to ensure the best available information is used.

As EPA gains more experience conducting TSCA risk evaluations for high priority chemicals, it would be useful if the Agency would develop a framework that articulates its process for deciding when conditions of use are in or out of scope. This would help EPA streamline future efforts, provide greater public understanding of EPA's decisions, increase transparency and reproducibility, and enable industry to identify the types of information that may be most helpful for manufacturers, processors, and downstream users to develop and/or share with EPA. Developing a framework would also help industry anticipate which conditions of use will be the likely focus in future assessments so that they can direct resources efficiently to develop and/or gather information relevant to EPA's potential risk evaluations and facilitate proactive data collection efforts.

C. EPA Should Coordinate Early With Other Appropriate Federal Executive Departments or Agencies.

Section 9(d) of TSCA imposes a general requirement on EPA to consult and coordinate with other federal agencies for purposes of "achieving the maximum enforcement" of TSCA while imposing the "least burdens of duplicative requirements on those [subject to TSCA]." This Section 9(d) coordination requirement has existed since TSCA was originally enacted and was unchanged by the 2016 amendments. Section 9(d) is a general policy directive that applies to EPA for all TSCA implementation activities. The risk evaluation rule also contains a general consultation provision that codifies the statutory requirement for interagency collaboration during the risk evaluation process.[7]

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[5] See Attachment A, American Chemistry Council Comments on the Application of Systematic Review in TSCA Risk Evaluations, Docket ID EPA-HQ-OPPT-2018-0210.
[6] EPA Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act, 82 Fed. Reg. 33726 (July 20, 2017).
[7] 40 C.F.R. § 702.39.

The principle driving this coordination requirement is that EPA should avoid imposing unnecessary or duplicative burdens on regulated entities and avoid regulatory actions best taken by another agency or under other EPA authority. This necessarily includes all manner of Agency interaction with regulated entities, including submission of information, docket management, responses to comments, and other engagement with multiple regulatory bodies. Where non-TSCA regulatory schemes are sufficiently effective at addressing risk, EPA may properly exclude covered conditions of use from the scope of the risk evaluation.

Regarding occupational exposures, EPA should consult early with OSHA in the risk evaluation process—certainly at the earliest stages of the risk evaluation and well before the scope is released.[8] This consultation should continue throughout the risk evaluation. None of the 10 problem formulations make clear what consultation may have occurred, or when it occurred. Although the problem formulations do identify available occupational exposure levels (OELs), i.e., PELs, TLVs, and IDLH values, additional information should be provided regarding the factors EPA will take into consideration when evaluating OELs. For example, consideration should be given to whether the OEL includes current toxicological and epidemiological data to support the development of the threshold limit value.[9] EPA also presents summarized personal monitoring air samples obtained from OSHA inspections, but it is not clear how these data were obtained from OSHA and under what circumstances the data were gathered. EPA should give preference to direct data obtained for uses being evaluated with consideration given to how the data were gathered (i.e., workplace exposure monitoring data are gathered on a more routine basis while OSHA monitoring is conducted typically in compliance with the OSHA Technical Manual for 8 hours and the sample will generally involve the scenario or tasks in which the highest exposure is expected).

For purposes of 9(d) compliance, it would be helpful if subsequent risk evaluation scopes offer more detail regarding EPA's coordination with other agencies, including information such as consultation plans, data shared, etc. We encourage EPA to include such a coordination plan in future scopes and to include these plans in the draft risk evaluations, including notations where consultation has occurred. It would be helpful for EPA to describe the decision criteria/framework by which it will evaluate whether to include occupational exposures in the scope of a risk evaluation. This description was not included in the 10 problem formulation documents.

D. EPA Must Use Tiered, Iterative Approaches to the Risk Evaluation Process.

EPA should apply a tiered approach throughout the risk evaluation process–from screening/prioritizing chemicals to conducting risk evaluations–under amended TSCA. This is essential to enable EPA to meet TSCA's statutory deadlines for completing risk evaluations,

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[8] To the extent that other regulatory authorities are relevant to a particular risk evaluation, the same principle of early consultation should apply. We focus on OSHA here due to the consideration of occupational exposure within the scope of all 10 problem formulations, although only nine will further analyze occupational exposure in the risk evaluation.

[9] Any OELs imposed by EPA as regulatory requirements must be ones that have been subject to notice and comment and suitable for regulatory purposes.

adhere to TSCA's robust scientific standards, and enable both EPA and the regulated community to apply limited resources efficiently.

When a screening-level assessment is insufficient to conclude a lack of risk to exposed populations, EPA should take steps to refine the risk evaluation allowing more accurate quantification of potential risks. The scoping/problem formulation documents indicate where the EPA feels it has sufficient information and where additional information and use of higher-tier tools is warranted. In situations where EPA may need to perform higher-tier assessments for the risk evaluation, more information is needed on the types of data and techniques that EPA will utilize. For example, EPA should indicate how probabilistic risk assessment (PRA), uncertainty analyses, and the use of statistical tools such as Bayesian statistics would be used at a higher tier within the overall problem formulation framework. A tiered, iterative approach is critical to the production of high quality risk evaluations based on the best available information.

II. Exposure Assessment Considerations

A. EPA Should Clearly Define How it Plans to Apply Tiered Exposure Assessments in TSCA Risk Evaluations, Beginning with the Initial 10 Chemicals.

Consistent with our recommendation above in Section I.D., EPA should apply tiered exposure assessments in its risk evaluations of high priority TSCA chemicals and clearly define its planned tiered exposure approach in EPA's problem formulation documents.

1. The Value of Tiered Exposure Assessments Is Widely Recognized.

The value of tiered exposure assessment is well-established. In its 1992 guidelines on exposure assessment,[10] EPA discusses the value of tiered exposure assessments from screening-level assessments to more complex assessments. This perspective was reiterated in EPA's 2016 peer review draft update of the 1992 guidelines.[11] The 2016 draft update included specific discussion of considerations in tiered assessments, as well as the notion of "fit for purpose" assessments, stating "[t]he type and purpose of an exposure assessment determine the data and information requirements."[12] The EPA Office of Research and Development (ORD) ExpoBox tool box for exposure assessors identifies exposure assessments tools by tier and type, both screening-level and refined, for planning, scoping, and problem formulation.[13]

The purpose of tiered exposure approaches is well understood: to identify uses of chemicals that, under very conservative (e.g., maximum) exposure assessment assumptions, are not likely to pose a health risk.[14] Depending on the conditions of use, the exposure assessment information

[10] US EPA, Guidelines for Exposure Assessment, Risk Assessment Forum, Washington, DC, EPA/600/Z-92/001, 1992.
[11] US EPA, Guidelines for Human Exposure Assessment, Risk Assessment Forum, Peer Review Draft, January 7, 2016.
[12] *Ibid*, at 2.
[13] https://www.epa.gov/expobox/exposure-assessment-tools-tiers-and-types-screening-level-and-refined.
[14] For example, see Patlewicz, G., et al. 2018. Utilizing Threshold of Toxicological Concern (TTC) with high throughput exposure predictions (HTE) as a risk-based prioritization approach for thousands of chemicals.

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can be used either to identify a chemical as a low priority or to be factored into the overall risk evaluation. Exposures that initially exceed hazard benchmarks in Tier-1 exposure assessments would require more refined, higher-tiered approaches to exposure assessments. This would include the application of more realistic parameters related to the likely duration, intensity, frequency, and number of exposures and more realistic exposure scenarios to more accurately quantify actual risks of the chemical.

The importance of EPA using a tiered approach to exposure assessment in its TSCA risk evaluations cannot be overstated. A tiered approach allows for both a more rapid, yet systematic, approach for assessing conditions of use in a first-tier screen, so that resources are used effectively when a refined exposure assessment is necessary for those conditions of use that do not "pass" a first-tier screen. A well-defined, tiered exposure approach can lead to greater efficiencies in chemical risk evaluations under TSCA. Congress clearly valued such efficiency highly as evidenced by the aggressive deadlines it set for EPA to conduct TSCA risk evaluations. Congress also directed the Agency to consider the likely duration, intensity, frequency, and number of exposures under the conditions of use.[15]

The value of tiered exposure approaches in risk evaluations is even broader than exposure assessment. This was discussed in the Health and Environmental Sciences Institute's (HESI) Coordinated Risk Assessment in the 21st Century (Risk21) project. A review article published in 2014 discussing Risk21's principles and framework for decision-making in human health risk assessment emphasizes that problem formulation for risk assessment should not be a hazard-driven process, but instead should start with exposure, focusing on exposure scenarios of greatest concern integrated with hazard information to support risk-based decision making.[16] The article suggests this approach would result in an early estimate of potential human exposure in relevant populations, including susceptible populations, which would characterize the degree of specific toxicological data needs.[17] The Risk21 framework also addresses two other principles: (1) additional data should be acquired "only if necessary and when they add value"[18] and (2) flexibility, "such that a higher tier hazard assessment approach can be coupled with a lower tier exposure approach, and vice versa."[19,20] Considerable progress has been made over the last several years in developing screening-level exposure prediction models for chemicals in commerce.[21] These approaches can be of particular utility in conducting Tier-1 assessments for many chemicals.

Computational Toxicology, 7: 58-67. Available at https://www.sciencedirect.com/science/article/pii/S2468111318300689

[15] 15 U.S.C. § 2605(b)(4)(F)(iv).

[16] Pastoor, T.P., et al. 2014. A 21st century roadmap for human health risk assessment. Critical Reviews in Toxicology, 44: 1-5. Available at https://www.tandfonline.com/doi/full/10.3109/10408444.2014.931923.

[17] *Ibid,* at 3.

[18] *Ibid.*

[19] *Ibid.*

[20] National Research Council. 2009. Science and Decisions: Advancing Risk Assessment. Washington, DC: The National Academies Press. Available at https://doi.org/10.17226/12209.

[21] For examples, see https://pubs.acs.org/doi/pdf/10.1021/acs.est.5b00498; https://pubs.acs.org/doi/abs/10.1021/es400482g; https://www.ncbi.nlm.nih.gov/pubmed/25222184

In the context of TSCA's risk evaluations, tiered-assessment concepts equip EPA with the tools it needs to meet TSCA's aggressive deadlines for completing risk evaluations of high priority chemicals. Tiered assessments also enable EPA to apply limited resources in an efficient manner. Using a clear, science-based tiered-assessment approach, EPA and the regulated community can perform exposure assessments in TSCA risk evaluations, enabling efficient decision-making.

2. A Road Map on Tiered Exposure Assessments Is Needed.

The draft problem formulation documents of the initial 10 chemicals mention the Agency's plans to use tiered exposure assessments in its risk evaluations of these chemicals, but the documents lack specifics. A clear "road map" showing EPA's approach to tiered exposure assessments is needed in EPA's scoping documents. Such a road map—or decision tree—would provide structure to EPA's approach to exposure assessments under TSCA. This structure would also be useful to explain how EPA will integrate the results of its tiered exposure assessments with the results from its tiered-hazard assessments in TSCA risk evaluations.

A road map would signal to the regulated community the type of reasonably available exposure information EPA plans to rely upon, what additional exposure information might be needed, and what actions manufacturers could take early in the risk evaluation process to provide EPA the needed exposure information. EPA should delineate what kinds of data and information it could accept to refine lower-tier exposure assessments.

Specifically, with respect to potential human exposures in the problem formulation documents, EPA should identify:

- The screening-level exposure information/models EPA will use to address human exposure in Tier-1 exposure assessments;
- The approach to hazard characterization and threshold EPA will use to ascertain the need for a higher-tier exposure assessment;
- How EPA will communicate Tier-1 exposure screening-level results;
- The higher-tiered information and models EPA will use to address human exposures, suggested by the results of the screening-level information/models;
- How EPA might use tiered exposure evaluations for specific exposure scenarios (e.g., occupational, consumer, residential, etc.)
- What kind of data and information EPA would accept (i.e. from stakeholders) to refine a Tier-1 screening exposure assessment.

3. EPA Guidance on Tiered Exposure Assessment Is Needed.

TSCA Section 26(l) requires EPA to develop "policies, procedures and guidance that the Administrator determines are necessary to carry out the amendments" of amended TSCA. EPA indicates its intent to use tiered approaches in TSCA risk evaluations, but guidance is needed. EPA should develop new, more specific guidance on its plans to use tiered approaches to exposure assessment in TSCA risk evaluations.

In doing so, EPA must move beyond mere "concepts" and reference lists to specific information, models, and tools. Specific and transparent guidance is needed to understand how the Agency will conduct its exposure assessments so that manufacturers can provide the most relevant information early on in the process to the Agency and so that stakeholders understand the process. As stated earlier, EPA should indicate how PRA, uncertainty analyses, and the use of statistical tools would be integrated as a higher tier assessment. Such guidance will also allow stakeholders to provide additional information to refine initial lower tier exposure estimates.

Further program-specific guidance is also needed for those manufacturers that plan to conduct risk evaluations for EPA's consideration and must conform to EPA's approach to risk evaluations should they do so. Guidance on tiered approaches will help streamline the risk evaluation process under TSCA and enable EPA to meet TSCA's new mandates.

Canada's Chemical Management Plan (CMP),[22] Australia's Inventory of Chemical Substances,[23] and the EU's Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH) program[24] employ tiered approaches in their exposure assessment approaches for chemicals. EPA should review those approaches to ascertain their usefulness in new EPA guidance on tiered exposure assessments in TSCA risk evaluations.

B. Occupational Exposures

According to EPA's problem formulations, EPA plans to further analyze occupational exposures in nine of the 10 chemicals risk evaluations. EPA must be more transparent about its coordination with OSHA regarding its plans to address occupational exposure issues in TSCA Section 6 risk evaluations. The methods, models, and databases that the Agency uses to conduct its occupational exposure assessments must be adequate to satisfy TSCA's Section 26 standards for best available science and weight of the scientific evidence. EPA should be more transparent about the OSHA and NIOSH databases that EPA plans to rely upon in these risk evaluations. Greater transparency will provide manufacturers notice about the type of information EPA may not have, but may need, to conduct a realistic occupational exposure assessment.

1. EPA Should Discuss in More Detail the Databases It Plans to Rely Upon in Its Occupational Exposure Assessments in Its Risk Evaluations.

In eight of the problem formulation documents, EPA has identified OSHA's Chemical Exposure Health Data (CEHD) and NIOSH's Health Hazard Evaluation (HHE) program data as two major sources of occupational monitoring data that it will rely upon in the risk evaluations. However, EPA does not discuss what information in these databases it plans to rely upon; how representative the data are; what criteria EPA will use in deciding which data are or are not applicable for its exposure assessments; or how it plans to assess those data in the context of

[22] https://www.canada.ca/en/health-canada/services/chemical-substances/fact-sheets/chemicals-management-plan-risk-assessment-toolbox.html
[23] https://www.nicnas.gov.au/__data/assets/word_doc/0018/35127/Inventory-Multi-tiered-Assessment-and-Prioritisation-Framework-Review-Document.docx
[24] https://echa.europa.eu/documents/10162/13632/information_requirements_part_d_en.pdf/70da6d4b-5acf-40d9-8b75-1e1c311378df

current OSHA regulations and industrial hygiene practices. EPA must provide greater detail about its use of the information in these OSHA and NIOSH databases to enable stakeholders to comment upon the data quality for the purposes for which EPA plans to rely upon the data, and to provide the Agency higher quality data where it exists.

For instance, it is our understanding that the OSHA CEHD information does not include a description of the activities associated with the specific exposure measurements. Without this information, how will EPA be able to apply these results to the conditions of use identified for a chemical? Absent sufficient knowledge of activities associated with occupational exposure measurements, EPA might very well improperly assign exposure values to a certain condition of use/application. This could result in inappropriate conclusions about risk under specific conditions of use or risk management recommendations for protection of workers. It appears that this database reports non-detects (ND), but it does not specify the limit of detection (LOD). Without an understanding of the accuracy of the data, how will EPA use this data to inform estimates of exposure?

In occupational settings, potentially hazardous exposures are eliminated or minimized by the use of training, industrial hygiene programs, engineering controls, closed systems, personal protective equipment (PPE), labeling, medical surveillance, etc. Over the past several decades, these engineering and industrial hygiene practices have continually improved. For example, as part of ACC's Responsible Care® Program, ACC member companies must implement ACC's Process Safety Code, which aims to supplement existing process safety requirements contained within the Responsible Care Management System® and RC14001® technical specifications. The Process Safety Code is intended to complement regulatory standards that, by necessity, focus on process safety at an individual facility.[25]

Another concern with the OSHA CEHD database is that much of the data were developed during inspections of facilities suspected of having high employee exposures. This suggests these data are not representative of occupational exposures from facilities that are in compliance with OSHA standards. EPA should address this fact in its quality review of the data/information underpinning its risk evaluations.

ACC understands that some ACC members have provided EPA with occupational monitoring information for use by the Agency in problem formulations for some of the initial 10 chemicals, but this information was apparently not reflected in the problem formulations issued on June 11, 2018. EPA should be clear in the draft risk evaluations how such submitted occupational monitoring information was used to prepare the problem formulations and considered in the risk evaluation.

[25] The ACC Process Safety Code is more universal, as it addresses issues across a division or corporation and includes a company commitment to set process safety expectations, define accountability for process safety performance, and allocate appropriate resources to achieve performance expectations. ACC members are required to demonstrate conformance to the Responsible Care management system as an obligation of membership. Conformance, including implementation of the ACC Process Safety Code, is demonstrated through ACC's mandatory third-party certification audit process.

2. EPA Should Provide Broader Guidance on How It Will Address Occupational Exposure Under TSCA.

EPA indicates it plans to further analyze occupational exposures in the draft risk evaluations in nine of the 10 problem formulations. EPA has conducted very few worker exposure assessments on existing TSCA chemicals in the past and its *Exposure Factors Handbook* does not address occupational exposures.[26]

EPA has occupational exposure tools that are designed for specific purposes. For example, ChemSTEER was developed as a conservative screening tool used to estimate workplace exposures and environmental releases for new chemicals that are manufactured and used in industrial/commercial settings. However, broad guidance is not currently available for evaluating occupational exposures under TSCA, in particular with respect to the evaluation of existing chemicals. EPA should develop new guidance for evaluating occupational exposures under TSCA.

To develop this guidance, EPA should certainly consider its own information, models, and tools on occupational exposure. EPA should also update some of its older tools and methods to evaluate worker exposure. EPA should update its 1997 Generic Scenarios for industry-specific workplace release and exposure estimation to make certain they reflect current industry practice. Many industrial practices in use today go beyond the legal regulatory requirements of OSHA. EPA should consider current industrial hygiene practices as part of the conditions of use of manufacturing. Additional Generic Scenarios may need to be developed to cover conditions of use for which Generic Scenarios do not currently exist.

It is also critical that EPA consider other information and tools available from OSHA, from the American Industrial Hygiene Association (AIHA), and from other jurisdictions to develop new occupational exposure guidance for TSCA purposes. EPA should consider the applicability of new models being used in Canada and the EU in their chemical regulatory programs.[27] In considering information and tools from OSHA, AIHA, and other jurisdictions, EPA should also consider the adequacy and appropriateness of use of those tools in the TSCA context.[28]

With respect to dermal exposures, the problem formulation documents identify several models for application to four of the 10 chemicals.[29] EPA's existing dermal exposure assessment guidance is primarily geared toward neat compounds in soil or water, and it is not clear whether this guidance is sufficient to evaluate chemicals encountered in industrial-use scenarios. For inhalation exposures, EPA has identified several models it plans to use in nine of the problem formulations.[30] EPA guidance on potential inhalation exposures in occupational conditions of use under TSCA would be helpful.

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[26] US EPA. Exposure Factors Handbook 2011 Edition (Final Report). Washington, DC, EPA/600/R-09/052F, 2011.
[27] For example, see ECHA's Advanced REACH Tool (ART) at https://www.advancedreachtool.com/.
[28] Any tools and information EPA would seek to adopt in its guidance should be available for notice and comment to ensure consideration public input.
[29] These include the ChemSTEER penetration model, ChemSTEER 2-Hand Dermal contact in Liquid; ChemSTEER 2 Hand Dermal Immersion in Liquid; PBPK model (Poet et al) and ChemSTEER
[30] These include the Near-Field/Far Field model (Keil); AEROMOD; EFAST; ChemSTEER; PBPK model (Poet et al); Two-Zone model; and Two-zone Near Field/Far Field (Jayjock et al.).

Guidance on occupational exposure assessment under TSCA should address how the Agency will consider standard industrial hygiene practices as well as how that information will be incorporated into its exposure assessments and how ultimately that information will be integrated into the risk evaluation. EPA should address and identify the specific information the Agency will need to accomplish these steps; the level of detail needed to enable the Agency to reach a determination about the adequacy of design measures such as: closed systems; the use of engineering controls and labeling requirements (e.g., the use of gloves or other PPE); and other operating procedures and management practices currently in use to eliminate or adequately minimize exposures in occupational settings. EPA should describe how these considerations are incorporated into a tiered occupational exposure assessment.

EPA may need to gather information from industry regarding current occupational exposure protection practices. Industry may be able to facilitate access to that information. Manufacturers and organizations like AIHA may be able to help the Agency gather information about exposure data in occupational settings and industrial hygiene practices in various workplace situations. Ultimately, through such efforts, an EPA exposure factors handbook for occupational exposures could potentially be developed to address TSCA risk evaluation needs. Consistent with application of a tiered approach to assessing exposure, EPA should articulate what kind of data will be acceptable to refine an initial lower tier occupational exposure assessment. For example, if a screening level estimate from ChemSTEER needs to be refined, a road map (as described above) would be a key element of guidance to develop the necessary information to conduct a higher tier assessment.

3. Greater Transparency Is Needed Regarding Exposure Models, Margins of Exposure and Occupational Exposure Limits.

EPA should be more transparent about specific exposure models, margins of exposure and occupational exposure limits that it intends to utilize during the risk evaluation process. This will allow stakeholders to provide the Agency the exposure information it needs and can lead to better understanding as to how EPA will make risk determinations.

As noted above in Sections I.D. and II.A.1, ACC agrees with EPA's support for using tiered approaches generally, and in exposure modeling in particular. Under a tiered, iterative approach, screening-level tools, which are "protective by design," may be used initially. For substances that appear to present potential risks following a screening-level assessment, EPA should then proceed to use higher-tier tools. By beginning with screening-level assessments—which use more conservative assumptions and information than higher tier models—the Agency can optimize resource allocation by identifying exposure routes that present less risk early in the assessment process. When a Tier-1 screening assessment indicates low risk for a particular condition of use, the Agency should have a high degree of confidence that the potential risks are lower or perhaps nonexistent.

It is critical that EPA establish clear and consistent guidance that defines when Tier-1 model results will trigger more detailed and refined subsequent assessments. The more rigorous models require more input data and more Agency resources, but will result in more realistic exposure

assumptions. In the problem formulation documents, EPA frequently cites regulatory and non-regulatory occupational exposure limits,[31] but it neither clarifies how it would apply these limits during an exposure assessment, nor specifies a process that will be followed should the Tier-1 model results exceed these limits or margins of exposure. In the event that EPA uses threshold triggers for Tier-2 models within EPA's risk assessment process, the Agency must provide guidance regarding how it selects these values and provide stakeholders an opportunity to comment.

Similarly, EPA should specify which exposure models—for all routes and populations—it intends to use during the risk evaluation process. In the problem formulations, EPA mentions several different models, but it does not provide rigorous guidance as to which tools will be used under which circumstances. Similarly, EPA does not identify specifically what it considers to be "higher tier models." Exposure models vary in terms of the purposes for which they are used, their input requirements, and assumptions. By providing a rationale for its model selection, the Agency will afford stakeholders an opportunity to provide appropriate data and contribute relevant information to EPA during its risk evaluations. EPA also should be clear about the use of modeled vs. measured data in evaluating exposure. For example, if measured data are rejected in favor of modeled estimates, the rationale for such a decision needs to be clear.

4. EPA Should Rely on Standard Exposure Scenarios to Improve Consistency Across the Agency's Exposure Assessments.

EPA participates in the OECD's Working Party on Exposure Assessment (WPEA). In that capacity, EPA has been a global leader helping harmonize chemical use categories and developing standard exposure/emission scenario documents (ESDs) for occupational exposure assessments for chemical regulations. ACC expects that EPA will use these standard exposure scenarios in its occupational exposure assessments, but that is not clear from the problem formulation documents. EPA should clarify this point in its draft risk evaluations of these 10 chemicals and in any new guidance the Agency develops on exposure assessments under TSCA.

In addition, EPA should develop additional standard exposure scenarios for both worker and consumer exposures under TSCA. Standard exposure scenarios would assure greater consistency in EPA exposure assessments; improve exposure model parameters; and help industry understand what specific information EPA needs in exposure assessments for TSCA risk evaluations. In short, standard exposure scenarios would improve efficiencies when conducting TSCA risk evaluations, which are critical given TSCA's statutory deadlines.

EPA may want to consider stakeholder workshops to discuss ways in which standard exposure scenarios might be developed in the US. If so, EPA should also ensure that standard scenarios developed under REACH be discussed and considered at such workshops since many of these may be useful in TSCA as well.

C. EPA Should Explain What Additional Ecological Exposure Assessment Tools Are Available.

[31] Common examples include, OSHA Permissible Exposure Limits (PELs), NIOSH Recommended Exposure Limits (RELs), or ACGIH Threshold Limit Values (TLVs).

The screening-level approaches described in the problem formulation documents are appropriate for this step (i.e., E-FAST), but EPA should identify acceptable tools/methods for higher-tier refinement when necessary. Screening-level exposure analysis may be suitable in cases where estimates do not exceed the Concentration of Concern (COC). EPA should explain how it would use higher-tier information, if provided.

EPA has indicated that environmental exposure data may be available for some of these 10 chemicals in the EPA Discharge Monitoring Report tool, EPA's STOrage and RETreival (STORET) system, USGS National Water Quality Assessment (NAWQA) program, and other sources. Some of these data sources may not be current and therefore may not represent the best available information. EPA should clarify exactly how it would use such data to establish a national, regional, or local environmental exposure estimate.

EPA should also clarify how it will quantify and assess (or exclude) naturally-occurring sources of chemicals for assessment during exposure estimation.

D. Consumer Exposures

1. All EPA Models Used in Its Assessments Must be Publicly Available and Accessible.

EPA's Consumer Exposure Model (CEM) is mentioned as the preferred tool for estimating consumer exposures in several of the first 10 chemicals' risk evaluations. This model is publicly available. However, another model mentioned by EPA is the Multi-Chamber Concentration and Exposure Model (MCCEM). This model is available on EPA's exposure tools website,[32] but in a version (Windows 95 operating environment)[33] that will not run on currently available platforms. EPA should ensure that all the models it uses in its assessments are publicly available in a form that is accessible to the general public, complete with explanations on how to use the model and how the exposure endpoints are estimated.

2. EPA Should Provide Greater Clarity about How It Will Assess Consumer Exposures to Chemicals in Products.

The problem formulations for most of the 10 chemicals indicate that the chemical is found in either formulated products used by consumers or in articles with which consumers could come into contact. It is not clear how EPA will assess consumer exposures to these products. The exposure assessments must be able to estimate the consumer exposures from these chemicals based on whether they are found in formulated products or articles.

For chemicals that are primarily in articles, the approach and rationale for estimating consumer exposures should be described in detail because exposure assessments from articles are a new area of assessment. Industry and other stakeholders may not be familiar with the rationale and approaches used to estimate exposures from articles. The scientific basis for determining

[32] https://www.epa.gov/tsca-screening-tools/approaches-estimate-consumer-exposure-under-tsca
[33] https://www.epa.gov/tsca-screening-tools/multi-chamber-concentration-and-exposure-model-mccem-version-12

exposures from chemicals in articles must be established for the Agency to meet the statutory standard that requires TSCA risk assessments to quantify the likely (i.e., having a high probability of being true) duration, intensity, frequency, and number of exposures under the conditions of use. EPA should clearly identify the criteria for and scope of the tools chosen to be used in each circumstance.

For exposure assessments, EPA may need to make decisions about which products to focus on in the assessments among the various potential products in which the chemical may be found. To conduct the consumer exposure assessment, the assessor may need to focus on representative products in some of these use categories. The product types chosen to be used in the exposure models, the exposure routes, most relevant exposure scenarios, exposure endpoints, and rationale for the choices must be described. The greater the clarity and transparency of these explanations, the greater the likelihood the final assessment will be understood.

E. Use of Toxic Release Inventory (TRI) Data

EPA states in several of the problem formulations that TRI data will be used as a source of information on releases to the environment. TRI data may have a role to play as an element in chemical prioritization, but these data also have limitations. EPA states on the TRI website:

> The Toxics Release Inventory (TRI) provides data about environmental releases of toxic chemicals from industrial facilities throughout the United States, measured in pounds. **The quantity of releases, however, does not indicate the level of health risk posed by the chemicals.** Although TRI data can't tell you whether or to what extent you've been exposed to these chemicals, they can be used as a starting point in evaluating potential risks to human health and the environment.[34] (Emphasis added.)

EPA readily acknowledges in its *TRI National Analysis 2016: Releases of Chemicals* that "[h]uman health risk resulting from exposure to toxic chemicals are determined by many factors…"[35] These factors include environmental fate, individual exposures, chemical properties, and concentration, none of which are furnished through the TRI. For a chemical to present a risk, there must be a sufficient pathway and exposure, factors that TRI does not address. EPA should acknowledge and explain the limited value of TRI data in risk evaluation.

F. Use of Biomonitoring Data

Biomonitoring information is identified in several of the problem formulations as a type of data/information source for TSCA risk evaluations, but there is limited discussion of how or where it would be used. EPA should address in guidance the specific biomonitoring information it would rely upon in TSCA risk evaluations and how it would be used.

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[34] Taken from https://www.epa.gov/toxics-release-inventory-tri-program/tri-and-estimating-potential-risk.
[35] TRI National Analysis 2016, www.epa.gov/trinationalanalysis/, January 2018, Releases of Chemicals p.6.

Canada uses "biomonitoring equivalents" in its risk assessments under the Canadian Management Plan (CMP).[36] EPA should examine how those values, as well as Canada's assessments that are based upon them, might be used in the TSCA exposure assessments.

III. Hazard Assessment Considerations

A. Integrated Hazard Assessment and Use of Non-Animal Methods

It is important that a multidisciplinary review process, which integrates hazard information and data from *in vitro* and *in vivo* studies across different biological levels of organization for a given exposure scenario, be established for hazard evaluation, data review, and decision making contexts. Typically, this should be a transparent and structured analysis using the Bradford Hill causal considerations and, in particular, biological plausibility and empirical support (dose response, temporal concordance and consistency). The hazard information must be relevant to the specific exposure scenario and the integration of data should be applied initially for each data stream (epidemiology, *in vivo*, mechanistic) across similar types of study endpoints. The lines of evidence (human epidemiology, *in vivo* toxicity and mechanistic) must then be integrated using a transparent and objective approach.[37] Through such an integrated assessment, evaluators use the entire body of studies and the full weight of the scientific evidence. This approach avoids the pitfalls of selecting the lowest statistically significant finding of a response in a given study (as a default) without adequately framing the risk hypotheses and integrating data from different sources.

EPA states in the general response to comments on the initial 10 scope documents that it anticipates using data from alternative test methods for the risk evaluations.[38] This is consistent with the mandate under TSCA Section 4(h) to "reduce and replace, to the extent practicable, scientifically justified, and consistent with the policies of this title, the use of vertebrate animals in the testing of chemical substances or mixtures…"[39]

ACC supports EPA's continued efforts to identify, develop, and integrate new approach methodologies (NAMs) for regulatory decision-making according to the EPA OPPT *Strategic Plan to Promote the Development and Implementation of Alternative Test Methods*.[40] It is important that sufficient scientific confidence in each NAM be established for its intended application before use as a key piece of evidence in a hazard evaluation and limitations be acknowledged.[41] It is equally important that exposure information, at a fit-for-purpose level of resolution, is available to place these data into a risk context.

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[36] https://www.canada.ca/en/health-canada/services/chemical-substances/fact-sheets/human-biomonitoring-data-risk-assessment.html.

[37] Rhomberg, L.R., et al. 2013. A survey of frameworks for best practices in weight-of-evidence analyses. Critical Reviews in Toxicology, 43(9): 753-84.

[38] https://www.epa.gov/sites/production/files/2018-06/documents/rtc_10_pf_53118.pdf

[39] 15 U.S.C. § 2603 (h).

[40] https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/strategic-plan-reduce-use-vertebrate-animals-chemical

[41] *Ibid.*

B. Analysis of Mode of Action (MOA)

EPA acknowledges that it must further analyze the MOA for cancer risk in the problem formulations. ACC supports that analysis.

The Adverse Outcome Pathway (AOP) framework can be employed specifically as an organizing principle elucidating MOA and connections to adverse outcomes. The AOP framework is a tool to systematically organize available data and knowledge that describes scientifically plausible and causal relationships across multiple levels of biological organization between a molecular initiating event (MIE) and subsequent key events (KEs), culminating in an adverse outcome (AO) potentially relevant to risk assessment.[42] EPA researchers have been instrumental in developing AOPs and tools to facilitate the further development, review, and use of AOPs in scientific and regulatory endeavors.[43] Tools such as the AOP wiki can be mined for additional data and organizational principles as well as domains of applicability for various identified MOAs associated with chemicals.[44] Thus, whether evidence generally aligns or does not align with any proposed or known MOAs and/or AOPs should be a necessary consideration in integrating evidence to reach conclusions.

The Agency's focus on dose-response data and models reflects the fact that toxicology has evolved over the past 35 years from a largely observational field of study to a discipline that applies advanced scientific techniques and knowledge to investigate how chemicals interact with biological systems at the molecular, cellular, organ, and organism levels to understand the biological basis for the induction of toxicity. As a consequence of rapid advances in scientific understanding and the application of this knowledge to regulatory science policy and risk assessments, risk assessors can now evaluate biological events leading to toxicity and consider how, in a dose-response manner, these events relate to potential risks to human health. Despite the significant progress, movement away from default assumptions has been slow to occur, particularly in certain EPA programs. Failure to recognize and act on advances in scientific knowledge and the best available, most relevant scientific data and dose response models wastes significant research and development investments. It is also contrary to the TSCA Section 26 requirement that EPA rely upon best available science in science-based Section 6 decisions.

In its 2005 Cancer Guidelines, EPA is clear that when risk assessments are performed using only one set of procedures, it may be difficult for risk managers to determine how much health protection is built into a particular hazard determination or risk characterization.[45] EPA's Cancer 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

[42] Ankley, G.T., et al. 2010. Adverse outcome pathways: a conceptual framework to support ecotoxicology research and risk assessment. Environmental Toxicology & Chemistry, 29(3): 730-741. doi: 10.1002/etc.34.
[43] https://www.epa.gov/sites/production/files/2017-03/documents/aop_research_brief_03_2017.pdf
[44] https://aopwiki.org/aops
[45] US EPA, Guidelines for Carcinogen Assessment, Risk Assessment Forum, Washington, DC, EPA/630/P-03/001F, March 2005.

> may decide to give greater weight to one set of procedures than another in a specific assessment or management decision. [46]

In addition, the Agency says:

> 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. 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.[47]

EPA's Office of Pesticide Programs (OPP) has adopted the World Health Organization (WHO)/International Programme on Chemical Safety (IPCS) MOA framework for organizing, evaluating, and integrating hazard and dose response information.[48] The same approach should be adopted for TSCA assessments. 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. To reliably predict toxicity, key events need to be causally linked to adversity with a clear understanding of dose response/temporal key event relationships. EPA should adopt and use the standard MOA templates for both cancer and non-cancer endpoints, such as the dose/temporal concordance and species concordance templates. These templates have been incorporated by the European Chemicals Agency (ECHA) in implementing Europe's REACH program.[49]

Because the scientific justification for assessing human relevance and selecting dose-response extrapolation methods for quantifying risks at environmentally relevant levels of exposure is highly dependent upon the determination of the likely operative MOA, the Agency should implement a uniform, systematic and explicit approach for evaluating a chemical dataset, using hypothesized MOAs and the evolved Bradford Hill causal considerations, to integrate evidence and derive weight of the evidence (WOE) confidence scores for potentially relevant MOAs.[50] This approach enables a side-by-side comparison of numerical WOE confidence scores for different hypothesized MOAs, including the default linear-no-threshold model, which permits better identification of the likely best MOA to use. The side-by-side quantitative MOA WOE confidence scoring method enhances transparency and improves communication amongst risk managers and the public. Furthermore, the best available science approach provides a

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[46] *Ibid,* at I-8.
[47] *Ibid*, at I-9.
[48] http://www.oecd.org/chemicalsafety/risk-assessment/iata-integrated-approaches-to-testing-and-assessment.htm
[49] https://echa.europa.eu/documents/10162/22315482/whoipcs_moa_template_withinstructions.docx/b98feba9-a37c-489d-94b0-dd5fbb2ed468
[50] Becker, R.A., et al. 2017. Quantitative weight of evidence to assess confidence in potential modes of action. Regulatory Toxicology & Pharmacology, 86: 205-220. doi: 10.1016/j.yrtph.2017.02.017

transparent, scientifically sound justification for using the most likely operative MOA as the basis for selecting the most appropriate extrapolation method that corresponds to that MOA to then calculate potential risks to humans for environmentally relevant exposures.

To illustrate this method, a case example has been developed based on data of rodent liver tumors induced by carbon tetrachloride (Attachment B). This case example used data and lines of evidence from previously published review articles, and relied on those authors' evaluations of the quality of the empirical evidence. Two hypothesized MOAs were evaluated: 1) induction of rodent liver tumors via a mutagenic MOA; and 2) induction of rodent liver tumors via a cytotoxicity MOA.

The quantitative MOA WOE confidence scoring results of this case example indicate:

- It is highly unlikely that carbon tetrachloride induces rodent liver tumors via a mutagenic MOA; and
- Cytotoxicity and sustained regenerative cellular proliferation is the likely operative MOA for induction of liver tumors in rodents by carbon tetrachloride; there are significant mechanistic data to support this non-linear, non-mutagenic MOA

Based on the comparison of quantitative MOA WOE confidence scores, there is strong scientific support for using a threshold extrapolation approach for evaluating the cancer risks of carbon tetrachloride. (In contrast, scientific justification is lacking to support a linear, no threshold extrapolation method for evaluating its cancer risks.)

Finally, another challenge in extrapolating animal data to human data involves having an understanding of the relative toxicokinetics. Significant strides have been made using physiologically based pharmacokinetic (PBPK) data and models in risk assessment to improve the accuracy of deriving dosimetry considerations.[51] However, it is important to recognize that some animal studies using conventional maximum tolerated doses (MTDs) are flawed and cannot be used to extrapolate to human doses because they exceed the kinetically-derived maximum dose (KMD). In a number of cases, substances show dose-dependent transitions in their mechanisms of toxicity.[52,53,54] This circumstance needs to be evaluated appropriately.

C. Ecological Hazard Characterization

EPA has used a simple approach to calculate the acute and chronic COCs, i.e., dividing the lowest study value by an assessment factor. Conservative, screening-level approaches, such as those utilized in the EPA's New Chemicals Program, can be appropriate to provide context at the problem formulation stage. However, in future scoping documents EPA should clarify the

[51] EPA discusses the need to evaluate available PBPK and empirical kinetic models for route-to-route and interspecies extrapolation of the point of departure (POD) in several of the problem formulations.
[52] Slikker, W., et al. 2004. Dose-dependent transitions in mechanisms of toxicity. Toxicology & Applied Pharmacology, 201(3): 203-25.
[53] Slikker, W., et al. 2004. Dose-dependent transitions in mechanisms of toxicity: case studies. Toxicology & Applied Pharmacology, 201(3): 226-94.
[54] Saghir S.A., et al. 2012. Assessment of diurnal systemic dose of agrochemicals in regulatory toxicity testing--an integrated approach without additional animal use. Regulatory Toxicology & Pharmacology, 63(2): 321-32.

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circumstances under which further, higher-tier evaluation would be triggered, if necessary (e.g. species sensitivity distribution, etc.).

EPA should identify more sophisticated higher-tier approaches it may use for determining a hazard threshold, especially for data rich chemicals. Toxicity information, and when available, knowledge of mechanisms, are integrated with exposure-response models for risk-based environmental safety decision making. Within an environmental context, the assessment of safety does not end at the organism, but includes extrapolation to populations, communities, and ecosystems. For ecological risk assessment, the possibility of obtaining site-specific population data is a critical option for higher-tier assessment.

EPA should also consider the unique physico-chemical properties that can impact substances' pharmacokinetics and toxicity profiles, as well as their environmental fate and distribution.

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IV. Conclusion

ACC commends EPA on its efforts to gather the best available information for the problem formulation documents for the initial 10 chemicals undergoing risk evaluation under amended TSCA. EPA has demonstrated some screening-level assessment techniques that allow EPA to focus on the conditions of use that pose the greatest potential for risk. However, in situations where EPA may need to perform higher tier assessments for the risk evaluation, more guidance and information is needed on the types of data and techniques that EPA will utilize. This will enable industry to better understand how to provide EPA with the information it needs to perform high quality risk evaluations.

ATTACHMENT A

ATTACHMENT B

Attachment A

AMERICAN CHEMISTRY COUNCIL COMMENTS ON THE APPLICATION OF SYSTEMATIC REVIEW IN TSCA RISK EVALUATIONS

August 2018

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Executive Summary

The American Chemistry Council (ACC) appreciates the opportunity to provide comments on the U.S. Environmental Protection Agency (EPA) Office of Pollution Prevention and Toxics (OPPT) systematic review approach for chemical risk evaluations under the amendments to the Toxic Substances Control Act (TSCA).

ACC appreciates the effort for transparency and the progress toward documentation of the TSCA systematic review approach. However, there are some critical concepts and methodologies that remain to be discussed or fully developed in the current approach document. Following the consideration of initial comments received, and the further development of the approach in the draft risk evaluations for the first 10 chemicals, EPA should re-issue the systematic review document with updates and allow for additional review and stakeholder feedback.

ACC makes the following additional recommendations:

- **Data collection** – Within the data collection phase of systematic review, it is critical that EPA capture studies generated for regulatory purposes in order to be truly fit for purpose as part of the TSCA risk evaluation process.
- **Use of existing assessments** - EPA must conduct its own assessment of existing toxicity values as many are dated and were published without the benefit of systematic review. Doing so will enable EPA to consider available studies reflecting the best available science.
- **Study quality** - ACC appreciates EPA's intention to be highly transparent and consistent in its evaluations through the use of a quantitative scoring system. EPA should consider adding additional explanation of some of its proposed methods for study quality evaluation to increase transparency.
- **GLP -** EPA should ensure that the study quality evaluations retain consideration of the robust study designs and highly documented processes required for studies conducted using EPA/OECD test guidelines in accordance with GLP regulations.
- **Selection of key studies** - EPA should provide additional information highlighting how study quality and relevance will be considered in selection of key studies for derivation of toxicity criteria and in forming overall conclusions.
- **Mode of action (MOA) and mechanistic data** - EPA should add an explanation of the importance of incorporating information on MOA and mechanistic data in problem formulation.
- **Evidence Integration** - EPA should use a transparent process to integrate evidence that is standardized in such a way that ensures consistent use of best available science and weight of the evidence.

I. Introduction

On May 31, 2018, the United States Environmental Protection Agency's (EPA's) Office of Pollution Prevention and Toxics (OPPT) released the systematic review approach for chemical risk evaluations under the amendments to the Toxic Substances Control Act (TSCA).[1] The document is intended to outline the general principles guiding EPA's application of systematic review in the risk evaluations for the first 10 chemicals, as well as other chemicals that will be evaluated in the future. It is important that EPA's problem formulation documents be read in consideration of EPA's systematic review approach. ACC[2] has filed comments on the problem formulation documents for the first 10 chemicals in each of the dockets. These comments are attached and incorporated by reference.[3]

ACC appreciates the transparency and progress toward documentation of the TSCA systematic review approach. EPA has developed a strong baseline systematic review approach, emphasizing the importance of allowing for "fit-for-purpose" evaluations tailored to specific substances and an iterative evaluation process. The guidance outlined for data searches, data screening, and data extraction is comprehensive and useful. Notably, the current guidance has a strong focus on study quality, and thoroughly outlines the proposed steps for study quality evaluation for each domain of evidence.

However, there are some critical systematic review concepts and methodologies that remain to be discussed or fully developed in the current approach document, most notably for the process of evidence integration. Following the consideration of initial comments received, and the further development of the approach in the draft risk evaluations for the first 10 chemicals, EPA should re-issue the systematic review framework document with appropriate updates and allow for additional review and stakeholder feedback. In particular, at that time, EPA should put forward the standardized procedures the Agency will use for integrating evidence that ensures consistent use of best available science, weight of the scientific evidence, and, as applicable, an understanding of mode of action (MOA).

The systematic review process should have sufficient flexibility such that it can adapt to the realities of the chemicals being tested and the limitations in experimental methodology and laboratory techniques. For example, the challenges in collecting hazard, fate, and exposure data for chemicals with any one of a number of characteristics which make them "difficult

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[1] US EPA, Application of Systematic Review in TSCA Risk Evaluations (Final). Office of Chemical Safety and Pollution Prevention, Office of Pollution Prevention and Toxics, EPA Document # 740-P1-8001. Available at https://www.epa.gov/sites/production/files/2018-06/documents/final_application_of_sr_in_tsca_05-31-18.pdf

[2] The American Chemistry Council (ACC) represents the leading companies engaged in the business of chemistry. ACC members apply the science of chemistry to make innovative products and services that make people's lives better, healthier and safer. ACC is committed to improved environmental, health and safety performance through Responsible Care®; common sense advocacy designed to address major public policy issues; and health and environmental research and product testing. The business of chemistry is a $768 billion enterprise and a key element of the nation's economy. It is among the largest exporters in the nation, accounting for fourteen percent of all U.S. goods exports. Chemistry companies are among the largest investors in research and development. Safety and security have always been primary concerns of ACC members, and they have intensified their efforts, working closely with government agencies to improve security and to defend against any threat to the nation's critical infrastructure.

[3] See Attachment A.

substances" for testing purposes are well known. Results from common adaptations of typical test methods for difficult substances should not be blindly rejected but should be subject to expert judgment to confirm the validity and applicability of such data.

Below, we provide comments on the EPA systematic review approach, as well as specific suggestions on concepts and methodologies that EPA should consider as it continues to develop the TSCA systematic review process.

II. Problem Formulation and Data Collection

EPA begins its systematic review approach document by re-emphasizing TSCA's focus on clear problem formulation. The importance of problem formulation in systematic review is well documented and supported.[4,5] The objectives and relevant scientific question(s) for chemical hazard, exposure, and risk assessment are often complex and require thoughtful consideration prior to and throughout each evaluation. Further, the problem formulation step is vital for identifying critical concepts and potential issues that may be faced later in the risk evaluation process.

EPA should add discussion emphasizing the importance of incorporating information on MOA data in problem formulation, and consider organizing the problem formulation step around these data, even if the MOA is not entirely clear from the outset. Existing frameworks, such as the World Health Organization (WHO)/International Program on Chemical Safety (IPCS) MOA/Human Relevance (HR) Framework,[6,7,8,9] the Adverse Outcome Pathway (AOP) framework,[10] or other similar approaches may be useful.[11]

Within the problem formulation phase of the evaluation, EPA must clearly describe any decisions regarding its planned use of other EPA office or agency assessments of the chemical under review. Further, OPPT should not automatically adopt existing toxicity criteria in the absence of its own review and consideration of possible alternative values using the proposed

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[4] Rhomberg, LR, *et al.* 2013. "A survey of frameworks for best practices in weight-of-evidence analyses." Crit. Rev. Toxicol. 43(9):753-784. doi: 10.3109/10408444.2013.832727.
[5] National Research Council (NRC). 2014. "Review of EPA's Integrated Risk Information System (IRIS) Process." National Academies Press. 204p. Accessed on May 06, 2014 at http://www.nap.edu/ catalog.php?record_id=18764.
[6] Boobis, AR, *et al.* 2006. "IPCS framework for analyzing the relevance of a cancer mode of action for humans." Crit. Rev. Toxicol. 36(10):781-792.
[7] Boobis, AR, *et al.* 2008. "IPCS framework for analyzing the relevance of a noncancer mode of action for humans." Crit. Rev. Toxicol. 38(2):87-96.
[8] 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. doi: 10.1002/jat.2949.
[9] Meek, ME, *et al.* 2003. "A framework for human relevance analysis of information on carcinogenic modes of action." Crit. Rev. Toxicol. 33(6):591-653.
[10] OECD Guidance document No. 184, Revised Guidance Document on Developing and Assessing Adverse Outcome Pathways. Available at http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2013)6&doclanguage=en
[11] For example, see Borgert, CJ; Wise, K; Becker, RA. 2015. "Modernizing problem formulation for risk assessment necessitates articulation of mode of action." Regul. Toxicol. Pharmacol. 72(3):538-551. doi: 10.1016/j.yrtph.2015.04.018.

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systematic review approach. We support EPA's intention, as specified in the problem formulation documents, to conduct its own independent assessment of existing toxicity values. In many cases, these existing reviews are dated and were published without the benefit of systematic review and consideration of available studies reflecting the best available science that have been more recently developed.

Regarding the data collection phase, the current approach for data searching, screening, and extraction is well developed. EPA provides detailed information on its plans to use specific search strategies and databases, how decisions will be made regarding screening (in both the abstract/title and full text screening phase), and how it will carry out the quality assurance (QA)/quality control (QC) process for all three parts of data collection. Further, EPA includes example search and screening strategies used for the first 10 chemicals, which provide helpful context on the implementation of this phase of the risk evaluation.

EPA's consideration of grey literature, such as technical reports, conference proceedings, and unpublished industry data, is well supported, as there are many sources that may be useful that have not been published in peer-reviewed journals. In order for this approach to be truly fit for purpose, it is critical that EPA capture studies generated for regulatory purposes at the data collection stage.[12] EPA should also consider the possibility of publication bias in the peer-reviewed literature; i.e., the possibility that studies with negative findings may not have been published.

ACC supports EPA's recommendation that the Agency pilot test the search and screening methods, which will be important for iterative evaluations. This will allow for changes to be made if it becomes clear that references have been missed by the use of specific search terms, or if relevant articles are being unintentionally screened out. Further, it is critical that EPA thoroughly describe the reasoning for any changes to risk evaluations resulting from pilot testing or other iterative phases of the assessment. Clarification is also needed as to how EPA will carry out iterative methods in later phases of an evaluation.

III. Data Evaluation and Integration

A. Application of Study Quality Criteria

Overall, the systematic review approach covers essential aspects of evaluating study quality. It indicates that EPA intends to thoroughly evaluate and fully consider the implications of the quality and relevance of the available evidence before incorporating it into its risk evaluations.

There are many positive attributes in the methods EPA describes, such as a training phase for reviewers to ensure consistency across quality evaluations. The specific criteria are informed by several existing, well-regarded evaluation systems that detail critical study quality and reporting criteria systems, such as the Strengthening the Reporting of Observational Studies in

[12] For example, OECD eChemPortal can serve as a resource: https://www.echemportal.org/echemportal/index.action

Epidemiology (STROBE) statement[13] and the Biomonitoring, Environmental Epidemiology, and Short-lived Chemicals (BEES-C) instrument.[14]

The study quality evaluation process appears to be very time intensive, and it is unclear whether it is possible to complete it in full for every evidence type for each evaluation, given the tight regulatory deadlines under TSCA. It is also unclear whether, as an alternative, EPA may rely on existing quality evaluations, and, if so, how these evaluations will be evaluated to ensure they adequately fulfill the rigorous quality assessment requirements proposed for TSCA evaluations. Also, as discussed below, EPA should consider adding additional explanation of some of its proposed methods to increase transparency. As it is difficult to determine how some aspects of the study quality evaluation system will operate in practice, EPA should solicit and consider additional feedback on the performance of the study quality criteria approach as applied in the initial risk evaluations.

1. Evaluation Method

Page 33 of the systematic review approach states, "EPA/OPPT plans to use data with an overall quality level of High, Medium, or Low confidence to quantitatively or qualitatively support the risk evaluations, but does not plan to use data rated as Unacceptable." ACC agrees that unacceptable data should not be used in the risk evaluation. There is some concern that low confidence studies could be used to quantitatively support a risk evaluation. If there is low confidence in the study methods and/or reporting, then it should not be used to quantitatively support the derivation of a point of departure in a hazard assessment. Rather, it should be used qualitatively as a supporting study or in a weight-of-evidence determination for hazard characterization.

EPA states that it will not automatically assign lower confidence to studies not adhering to Good Laboratory Practice (GLP) or Organisation for Economic Co-operation and Development (OECD) guidelines, but rather, it will consider, "any and all available, relevant data and information that conform to the TSCA science standards" as acceptable.[15] What this might mean for academic studies, which are usually not conducted according to GLP requirements and may use non-standard methods, is unclear. EPA should ensure that the study quality evaluations retain consideration of the robust and highly documented process required by GLP guidelines, even if they are not GLP studies. As noted by Borgert et al., 2016, "…regulatory agencies have placed a high value on study reports that include sufficient detail to allow reanalysis of data to independently confirm results and support additional analysis using alternative methods of data evaluation."[16]

Borgert and co-authors also emphasize that GLP-compliance is much more than record keeping and reporting.

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[13] von Elm, E, *et al.* 2007. "Strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies." BMJ 335(7624):806-808.
[14] LaKind, JS, *et al.* 2014. "A proposal for assessing study quality: Biomonitoring, Environmental Epidemiology, and Short-lived Chemicals (BEES-C) instrument." Environ. Int. 73:195-207. doi: 10.1016/j.envint.2014.07.011.
[15] US EPA, Application of Systematic Review in TSCA Risk Evaluations (Final), at 32.
[16] Borgert, CJ, *et al.* 2016. "Does GLP enhance the quality of toxicological evidence for regulatory decisions?" Toxicol. Sci. 151: 206–213. Available at https://academic.oup.com/toxsci/article/151/2/206/2241188

> GLP requires justification of the test system and procedures; training certification and documentation for investigators and technicians involved in each scientific procedure; the measurement of a comprehensive set of study parameters, including: analytical characterization of test materials; analytical verification of concentration, stability, and homogeneity of dosing solutions; validation and calibration of instruments; adherence to standard operating procedures in conducting experimental activities; independent auditing of study procedures and data; adherence to animal welfare requirements; measurement of laboratory and animal room conditions, among many other important assurances of experimental quality. The goal of these requirements is to ensure that critical study parameters—parameters that go to the core of study quality—are, in fact, measured. Furthermore, GLP requires that a study protocol be selected and justified a priori, that any deviations from that protocol occurring during the study are documented with appropriate written explanation or justification, and that these elements are audited by an independent party before finalization of the study report. [...] In particular, GLP specifically meets their requirements for carefully recorded and audited data covering relevant exposure routes and doses.[17]

2. Scoring Method

Overall, the scoring examples shown are clearly and transparently laid out in a series of tables. The weighting scheme, metrics, and overall scoring are relatively straightforward. ACC appreciates EPA's intention to be highly transparent and consistent in its evaluations through the use of a quantitative study scoring system. However, the scoring system described in the current approach is complicated by many possible options that may or may not be used, such as weighting factors. This may result in very specific scores with a relatively narrow range, which may make interpreting studies of similar but not identical quality difficult (e.g., a score of 1 versus 1.7). Further, some of the weighting factors chosen involve substantial scientific judgment, and EPA should consider that some metrics may be more important to overall quality for specific studies, relative to others, indicating that a generic "one-size-fits-all" weighting factor could become problematic. For example, in the criteria for occupational exposure and release data evaluation, it is unclear why the metric of methodology in the reliability domain is given a weighting factor of 1, when other critical factors, such as reliability, are weighted at 2. Incorrect or inappropriate methodology could be just as critical of a flaw, if not more so, than some of the other metrics.

In addition, while the use of a 1-4 scale for judging whether a study is evaluated to have high confidence, medium confidence, low confidence, or be unacceptable for use is clearly laid out and justified, it is anticipated that there could be some confusion with the already much-used Klimisch system of study evaluation.[18] The Klimisch system is somewhat similar in that studies assigned a 1 or a 2 are considered reliable without restrictions, or reliable with restrictions, respectively. However, the Klimisch system differs from the one EPA is proposing by

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[17] *Ibid*, at 208.

[18] Klimisch, HJ, *et al.* 1997. "A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data." Regul. Toxicol. Pharmacol. 25:1-5.

attributing a score of 3 to studies that are not reliable, and a score of 4 designating a score is not assignable due to insufficient information. In other words, the scale used on EPA's approach is the opposite of the Klimisch system for scores of 3 and 4. Furthermore, Klimisch scoring does not use weights or calculate mathematical averages, but rather assigns qualitative overall integer values of 1, 2, 3, and 4. Since the Klimisch scoring is already broadly used in regulatory activities across the globe, EPA should consider harmonization for evaluating studies in order to avoid confusion and harmonize with other geographies.

3. Data Availability

The availability of data and other information required to verify and reproduce critical studies in the risk evaluation is also important. Any data that are used to derive toxicity criteria should be made publicly available to the greatest degree possible, while still protecting confidential business information (CBI) and other sensitive personal information, consistent with EPA's recently proposed rule on Strengthening Transparency in Regulatory Science.[19] This will facilitate transparency and allow others to consider and independently evaluate the quality, reliability, and interpretation of these data. For example, a frequent concern with published academic studies is that the data presented in either tabular or figurative form have already experienced some form of statistical transformation. In many cases, even an expert-level statistician cannot recreate the original data from these data.

Academic laboratories sometimes conduct their statistical analysis using laboratory personnel who are not professional statisticians. The technical issue with non-professional analysis is rarely whether the test was conducted correctly, but rather whether the most appropriate statistical test was selected. In a seminal study conducted by Begley and Ellis (2012), the study authors were unable to replicate the results from statistical analyses of 47 of 53 landmark pre-clinical cancer research papers.[20] This led to a flurry of other studies in different fields that have also reported similar findings. Thus, it is crucially important that data upon which regulatory actions are based be available for independent statistical analysis.

B. Evidence Integration

In the current systematic review approach document, the strategy for evidence 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 recognizes that the evidence integration phase of assessments is underdeveloped and indicates that it anticipates defining and demonstrating the process of integration in the forthcoming first 10 chemical draft risk evaluations. We expect that as EPA gains more experience with evidence integration, and can describe the standardized procedures the Agency will use for integrating evidence that ensures consistent use of best available science, weight of the scientific evidence, and, as applicable, understanding of MOA, the Agency will revise this guidance document. Such a

[19] See 83 Fed.Reg. 18768 (April 30, 2018). ACC has filed comments on this proposed rule at Docket ID: EPA-HQ-OA-2018-0259.
[20] Begley, CG; Ellis, LM. 2012. "Drug development: Raise standards for preclinical cancer research." Nature 483(7391):531-533. doi: 10.1038/483531a.

revision should include additional review and public comment. Below, we describe methods and concepts that EPA should consider as it further develops the approach to evidence integration.

1. General Methodology

First, EPA should use a transparent process to integrate evidence that is standardized in such a way to allow for greater efficiency. EPA should consider development of a structured narrative that fully describes how the different pieces of available evidence support a given conclusion/argument or an alternative.[21,22] In this way, EPA can clearly demonstrate how specific studies or data sources contributed to the final conclusion. This will ensure that the process by which EPA reaches conclusions about exposure, hazard, and/or risk will be well developed and transparent.

Second, as a part of the evidence integration narrative, EPA should clearly describe how the study quality evaluations will be used to weigh the evidence and reach conclusions for the different phases of the risk evaluation, including exposure assessments, hazard assessments, and any quantitative estimates of risk. For example, the current approach does not indicate whether a high-confidence study will always be given more weight than a medium-confidence study in formulating conclusions, or how other factors, such as study relevance, will be weighed with quality considerations. EPA should consider building from the published approaches for quantitative weight-of-evidence analysis, such as Bridges et al., 2017;[23] Becker et al., 2017;[24] and Dekant et al., 2017.[25]

Third, EPA should detail how it will conduct uncertainty analyses and communicate these uncertainties consistently and transparently in each risk evaluation.

2. Critical Concepts

While MOA/AOP evidence and mechanistic data are mentioned in several places in the systematic review approach, EPA should consider expanding its discussion of this important evidence, particularly in the evidence integration phase of evaluation. MOA/AOP evidence and mechanistic data should be weighed concurrently with observational and toxicology evidence and considered a critical organizing principle for the weight-of-evidence evaluation.

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[21] The National Academy of Sciences recommends templates for structured narrative justifications of the evidence-integration process and conclusions for the IRIS Program in the 2014 Review of EPA's Integrated Risk Information System (IRIS) Process, Committee to Review the IRIS Process; Board on Environmental Studies and Toxicology; Division on Earth and Life Studies; National Research Council, available at https://www.nap.edu/catalog/18764/review-of-epas-integrated-risk-information-system-iris-process.

[22] See also the guidelines for integrating evidence in Rhomberg, LR, *et al.* 2013. "A survey of frameworks for best practices in weight-of-evidence analyses." Crit. Rev. Toxicol. 43(9):753-784. doi: 10.3109/10408444.2013.832727.

[23] Bridges, J, *et al.* 2017. "Framework for the quantitative weight-of-evidence analysis of 'omics data for regulatory purposes." Regulatory Toxicology and Pharmacology 91 (2017) S46-S60.

[24] Dekant, W, *et al.* 2017. "A quantitative weight of evidence assessment of confidence in modes-of-action and their human relevance." Regulatory Toxicology and Pharmacology 90:51-71. doi: 10.1016/j.yrtph.2017.08.012.

[25] Becker, RA, *et al.* 2017. "Quantitative weight of evidence to assess confidence in potential modes of action." Regulatory Toxicology and Pharmacology 86:205-220.

The AOP framework can be employed specifically as an organizing principle that explains MOA and the connections to adverse outcomes. The AOP framework is a tool to systematically organize available data and knowledge that describes scientifically plausible and causal relationships across multiple levels of biological organization between a molecular initiating event (MIE) and subsequent key events (KEs), culminating in an adverse outcome (AO) potentially relevant to risk assessment.[26] EPA researchers have been instrumental in developing AOPs and tools to facilitate the further development, review, and use of AOPs in scientific and regulatory endeavors.[27] Tools such as the AOP wiki can be mined for additional data and organizational principles as well as domains of applicability for various identified MOAs associated with chemicals.[28] Thus, whether evidence generally aligns or does not align with any proposed or known MOAs and/or AOPs should be a necessary consideration in integrating evidence to reach conclusions.

Since the scientific justification for assessing human relevance and selecting dose-response extrapolation methods for quantifying potential cancer risks at environmentally relevant levels of exposure is highly dependent upon the determination of the likely operative MOA, the Agency should implement a systematic and explicit approach for evaluating a chemical dataset, using hypothesized MOAs and the evolved Bradford Hill causal considerations, to integrate evidence and derive weight of the evidence confidence scores for potentially relevant MOAs.[29] This approach enables a side-by-side comparison of numerical weight of the evidence confidence scores for different hypothesized MOAs, including the default linear no threshold model. This enhances transparency and improves communication among risk managers and the public. 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 to then calculate potential risks to humans for environmentally relevant exposures.

In addition, EPA should describe how it will consider issues of the adversity of identified health effects when considering the weight of the evidence. For example, there may be animal studies that demonstrate statistically significant effects that are reversible, and/or epidemiology studies may show changes in blood biomarkers but are not predictive of clinical disease. Results of this nature (those for which the adversity or clinical relevance is either questionable or unclear) should be interpreted with caution when making causal conclusions regarding hazard, and when selecting endpoints for consideration as critical effects.

Finally, EPA should add a discussion of how it will consider questions of relevance in the data evidence integration and summary phases of the risk evaluation. EPA indicates that it will use a tiered approach to check for relevance at various points in each risk evaluation, including during data screening and selection. However, it is not entirely clear how data will be weighed according to relevance when integrating evidence to support conclusions when presumably, at

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[26] Ankley, GT, *et al.* 2010. "Adverse outcome pathways: a conceptual framework to support ecotoxicology research and risk assessment." Environ. Toxicol. Chem. 29(3):730-741. doi: 10.1002/etc.34.
[27] https://www.epa.gov/sites/production/files/2017-03/documents/aop_research_brief_03_2017.pdf
[28] https://aopwiki.org/aops
[29] Becker, RA, *et al.* 2017. "Quantitative weight of evidence to assess confidence in potential modes of action." Regul. Toxicol. Pharmacol. 86:205-220.

this point in the evaluation, all evidence discussed was previously deemed relevant to the risk evaluation for some purpose.

3. Utilization of Existing Frameworks

EPA should consider reviewing and adapting portions of other established systematic review and weight-of-evidence frameworks. For example, one recent and generally well-developed framework is the European Food Safety Authority (EFSA) Guidance on the use of the weight-of-evidence approach in scientific assessments.[30] Critical concepts in weight-of-evidence are well described, including the consideration of relevance, reliability, and consistency within and across lines of evidence. Various options for causal frameworks are presented, and EFSA emphasizes that, in many cases, a single method often cannot cover all steps. Differing methods, or a combination of methods, may be needed for a given assessment. These fit-for-purpose decisions can be documented in the problem formulation phase of assessment and thus will be vetted via peer review and public comment.

4. Transparency

Transparency in the decision-making process is vital for producing scientifically defensible and understandable assessments. Clear, thorough discussions of all decisions will increase confidence and aid in the general acceptance of the findings and conclusions of TSCA risk evaluations. The transparency of overall conclusions on chemical hazard, exposure, and risk may also be enhanced by the use of tabular and/or graphical summaries of the weight-of-evidence conclusions. Further, it is important that in all phases of the assessment, but particularly in the evidence integration and summary sections of the assessment, EPA clearly describes all areas in which expert judgment was utilized.

IV. Conclusions

The EPA TSCA systematic review approach has many positive attributes, with several areas of guidance that have been very well developed. The approach focuses on fit-for-purpose evaluations and an iterative evaluation process, which allow for flexibility that is necessary given the wide array of chemical substances that will be reviewed under TSCA. However, there are several areas in the document that lack detail and specificity – most notably, evidence integration. In future iterations of the document and forthcoming risk evaluations, there should also be a more explicit discussion of several critical concepts, such as the use of MOA/AOP knowledge and mechanistic data and consideration of the adversity of effects.

In addition, it is unclear how the study quality evaluations will be fully incorporated into conclusions regarding hazard, exposure, and risk; the guidance document would benefit from additional discussion of its plans for this phase of analysis. Finally, it is critical that scientific judgment and iterative changes are transparent and justified in the final risk evaluations.

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[30] European Food Safety Authority (EFSA) Scientific Committee. 2017. "Guidance on the use of the weight of evidence approach in scientific assessments." EFSA J. 15(8):4971. doi: 10.2903/j.efsa.2017.4971.

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Overall, the EPA OPPT systematic review approach would benefit from additional explicit guidance, which will increase transparency within the EPA TSCA systematic review approach and ensure objective, comprehensive, scientifically supported risk evaluations for TSCA chemicals. The ability to replicate EPA's analyses, based upon the detailed guidance, will increase public confidence in risk evaluations conducted by the agency.

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Attachment B

IDENTIFYING THE LIKELY OPERATIVE MODE OF ACTION FOR CARBON TETRACHLORIDE INDUCED RODENT LIVER TUMORS

Scientific Causality Confidence Scores for Potential Modes of Action: Comparing the Weight of Evidence for a Mutagenic Mode of Action to a Threshold Cytotoxicity Mode of Action for Rodent Liver Tumors

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I. Executive Summary

Background: One of the critical elements of a chemical carcinogenic risk assessment is the determination of the likely operative mode of action (MOA). Determining the operative MOA by which a chemical can cause cancer is important for characterizing potential human health hazards and for selecting dose-response extrapolation methods for use in risk assessment at environmental levels of exposure. This case example focused on evaluating hypothesized MOAs involved in the induction of liver tumors in rodents by carbon tetrachloride.

This case example used the quantitative MOA WOE confidence scoring approach described in Becker et al., 2017[1]. This method provides a systematic and explicit approach for 1) evaluating a chemical dataset using hypothesized MOAs and the evolved Bradford Hill causal considerations (biological plausibility, essentiality, dose-response concordance, consistency, and analogy) and 2) deriving an overall confidence score for each hypothesized MOA. This enables a side-by-side comparison of numerical WOE confidence scores for each MOA, and the determination of which MOA is more likely to be operative.

Analysis and Results: Using the quantitative MOA WOE confidence scoring approach described in Becker et al., 2017 and data for carbon tetrachloride, we compared the WOE for a mutagenic MOA to the WOE for a threshold cytotoxicity MOA. We summarized the relevant dose-response and incidence data and developed WOE confidence scores for both a mutagenic MOA and a threshold cytotoxicity MOA (see sections III and IV for details).

This analysis indicates:

- It is highly unlikely that a mutagenic mode of action is plausible for carbon tetrachloride-induced rodent liver tumors. Based on the MOA confidence score of -36, the weight of evidence clearly does not support a mutagenic mode of action for carbon tetrachloride. The negative score indicates there is strong counter evidence for several of the early, diagnostic, KEs for a mutagenic MOA. In other words, the available data indicate that it is highly unlikely that rodent liver tumors are induced by carbon tetrachloride via a mutagenic mode of action

- The MOA causal confidence scoring results indicate that the more likely operative MOA is cytotoxicity and sustained regenerative cellular proliferation which exhibits a non-linear/threshold dose-response. Therefore, an increase in cancer risk would only occur at doses that exceed a specific threshold. There are significant mechanistic data to support a non-linear, non-genotoxic mode of action for carbon tetrachloride, and based on the MOA confidence score of +87, the weight of evidence clearly supports a cytotoxic mode of action for carbon tetrachloride induction of rodent liver tumors

Conclusions and Recommendations: Based on the weight of the evidence (indicated by comparison of the MOA confidence scores), the likely operative MOA is cytotoxicity, not mutagenicity. The overall pattern of observations is very consistent with a non-linear, threshold mode of carcinogenic action, as evident by the MOA confidence score of +87 for cytotoxicity compared to the mutagenic MOA confidence score of -36. Therefore, it would be inappropriate to use a linear default for extrapolating cancer risks. Instead, the causal weight of the scientific evidence analysis supports use of a threshold, non-linear method for determining potential cancer risks (i.e., an extrapolation method based upon cytotoxicity, for which cancer risk would only be operative at doses that exceed the threshold for induction of hepatic cytotoxicity).

[1] Becker RA et al., 2017. Quantitative weight of evidence to assess confidence in potential modes of action. Regul Toxicol Pharmacol. 86: 205-220. OPEN ACCESS: http://www.sciencedirect.com/science/article/pii/S0273230017300387?via%3Dihub

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As the Agency moves forward with its problem formulation and risk assessment of carbon tetrachloride, we encourage you to consider use of the quantitative confidence scoring method for determining and communicating the more likely operative MOA based on the weight of scientific evidence. This method provides a scientifically based WOE approach for selecting the most appropriate extrapolation method for determining potential human health risks. In fact, this approach should prove to be useful for most, if not all, of the TSCA assessments now being developed by OPPT that deal with potential carcinogenic risks, especially where alternative (non-mutagenic) MOAs with supporting mechanistic data are credible.

II. Introduction

One of the critical elements of a chemical carcinogenic risk assessment is the determination of the likely operative mode of action (MOA). Understanding a chemical's mode of carcinogenic action forms the scientific basis for the selection of the dose-response extrapolation method that best aligns with the underlying biology of the specific MOA pathway, and subsequently, ensures that the best available science is used for quantifying potential cancer risks at environmental levels of exposures.

To improve transparency and objectivity in MOA analysis, the WHO/IPCS MOA framework has recently been extended using an approach that enables quantitative scoring of the confidence in the weight of the evidence of alternative hypothesized MOAs. We have attached the abstract and link to the open access, peer-reviewed publication detailing this quantitative method (Appendix A. Becker *et al.*, 2017). As described in the publication, a systematic and explicit approach is used for evaluating a chemical dataset using key events in the context of the evolved Bradford Hill causal considerations, in order to integrate evidence and derive confidence scores for potentially relevant MOAs. This enables a side-by-side comparison using numerical scores of scientific confidence in each hypothesized MOA, including a default mutagenic MOA, to better identify the more likely (i.e., best supported) operative MOA. We are in the process of developing several additional case examples on a variety of chemicals to further illustrate the application of the MOA quantitative confidence scoring method and to support the continued refinement of the method.

As EPA commences the risk assessment of carbon tetrachloride, we believe the application of the quantitative MOA confidence scoring method can, as part of EPA's consideration of best available science and weight of the evidence, inform and strengthen the Agency's problem formulation phase of the cancer risk assessment.

The quantitative MOA WOE confidence scoring approach detailed in Becker et al., 2017 is a systematic and explicit approach for evaluating a chemical dataset, using hypothesized MOAs and the evolved Bradford Hill causal considerations (biological plausibility, essentiality, dose-response concordance, consistency, and analogy), to integrate evidence and derive confidence scores for potentially relevant MOAs. The components consist of: 1) a set of defining questions for each of the Bradford Hill considerations coupled with a WOE rating and scoring procedure to guide data evaluation and WOE determinations; 2) a procedure to score the evolved Bradford Hill causal consideration for essentiality at MOA pathway level based on the highest score achieved by any one of the unique Key Events (KEs) in the pathway; 3) a technique for including the supporting evidence of later KEs, even though these are disease-specific and not diagnostic of a MOA for a particular chemical, by affording less evidentiary value to later KEs than the earlier, more MOA-specific KEs; 4) hierarchical weighting of the evolved Bradford Hill causality considerations; and 5) a straightforward arithmetic method to characterize the overall confidence score for each hypothesized MOA.

To document the application of the recently peer-reviewed quantitative MOA WOE confidence scoring approach (Becker et al., 2017), we have developed this case example using the published carbon tetrachloride rodent liver tumor MOA data. The steps of quantitative MOA WOE confidence scoring are discussed in detail

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in Becker et al., 2017; they are briefly described here to help contextualize the case example tables presented in Sections III and IV.

- Step 1. Identification of postulated MOAs and KEs/KERs for the adverse outcome(s) of interest (See Section 2.1 of Becker et al., 2017). (Note: Steps 2 through 5 are conducted for each hypothesized MOA.)

- Step 2. Qualitatively evaluate the evidence in support of, or inconsistent with, the KEs/KERs (See Section 2.2 of Becker et al., 2017), using the evolved Bradford Hill causal considerations.

- Step 3. Quantitatively rate each KE/KER using the evolved Bradford Hill causal considerations (See Section 2.3.1 of Becker et al., 2017). In the qualitative and quantitative rating approach (Steps 2 and 3), the individual or series of KEs are evaluated against the defining question for each evolved Bradford Hill causal consideration, using the WOE rating categories to guide the determinations for scoring. The rating categories include strong (3), moderate (2), weak (1), no evidence (0), weak counter evidence (-1), moderate counter evidence (-2), and strong-counter evidence (-3).

- Step 4. Derive the composite score for each KE/KER by multiplying the quantitative rating score by the weight assigned for each of the evolved Bradford Hill causal considerations and adjust based on the MOA evidentiary value of each KE/KER ($\sum$ (weight $\times$ rate $\times$ evidentiary value) = KE/KER score) (See Section 2.3.2 of Becker et al., 2017). To derive the composite score, each Bradford Hill causal consideration has been given a numerical weight in accordance with their ranked importance, with a summed maximum of 100% (Section 2.3.1 of Becker et al., 2017). Essentiality of the KEs within the MOA is considered collectively since the interdependence of KEs is often illustrated through the impact of prevention or augmentation of an earlier KE on later KEs. Furthermore, all KEs/KERs are not necessarily weighted the same. This is because for a given adverse outcome, often the later KEs leading to the adverse outcome are the same for each of the hypothesized MOAs. These later KEs are often indicative of the disease process, whereas the earlier KEs are more chemical-specific and more influential in determination of MOA, so in this method the later KEs that are common across MOAs are assigned an evidentiary weighting value of 10%.

- Step 5. Integrate the evidence of causality for the MOA by calculating the sum of the scores for all KEs/KERs and then dividing by the total maximum score to derive the "MOA confidence score" (See Section 2.4 of Becker et al., 2017). To calculate the overall WOE confidence score for a hypothesized MOA, KE scores are summed and normalized by dividing by the maximum possible score and then multiplying by 100. This simple normalization procedure allows for comparison of quantitative confidence scores in cases where the number of KEs differs between hypothesized MOAs. Total scores may be negative if, for a hypothesized MOA, there is strong counter evidence for several of the early, most diagnostic KEs.

- Step 6. Compare the quantitative confidence scores for the hypothesized MOAs, and select the MOA for which confidence in the supporting data is highest (See Section 2.4 of Becker et al., 2017).

Using the quantitative MOA WOE confidence scoring approach, in Sections III and IV below, we have summarized the relevant dose-response and incidence data and developed WOE confidence scores for a mutagenic MOA and for a threshold cytotoxicity MOA.

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Note: The intent of this case study is to illustrate the quantitative scoring methodology. It is not intended to be a complete discussion of all available and relevant studies. To that end, we did not conduct an in-depth systematic review of the available literature, but we based this evaluation on data and lines of evidence from already published review articles, and those authors' evaluations of the quality of the empirical evidence. The data and lines of evidence used in developing this case example are from scientifically peer reviewed and journal published articles. For the development of this specific case example, the primary authors (LHP and MKM) developed the initial evaluation and an additional MOA expert (RAB) provided peer review of the interpretation and quantification of the MOA scores. As indicated in Becker et al., 2017, with respect to biological plausibility of hypothesized modes of action leading to cancer, both the mutagenic mode of action and the cytotoxic/regenerative cell proliferation mode of action are considered to be well documented, and thus the biological plausibility of these MOAs are not considered further herein. Rather, chemical-specific supporting data for the evolved Bradford Hill causal considerations (essentiality, dose-response, incidence and temporal concordance, consistency, and analogy) are specifically evaluated for the Key Events/Key Event Relationships (KEs/KERs) as a basis to apply the quantitative weight of evidence confidence scoring method.

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III. Evaluating the WOE for a Mutagenic MOA

Carbon Tetrachloride (CTC) has been investigated extensively over many years, both *in vitro* and *in vivo*, for evidence of genotoxicity/mutagenicity, in an attempt to demonstrate a key role for a DNA-reactive mode of action (MOA). The key events for a mutagenic MOA leading to hepatocellular carcinoma, identified based on a different chemical (Moore *et al.*, submitted), would be as follows for CTC:

1) Metabolism to a reactive intermediate leading to the formation of pro-mutagenic CTC-specific DNA adducts
2) Insufficient repair or mis-repair of pro-mutagenic CTC-DNA adducts
3) Early induced mutation in cancer critical genes in target tissue
4) Cellular proliferation, clonal expansion of mutant cells, and progression
5) Hepatocellular carcinoma (HCC)

Given the large number of genotoxicity/mutagenicity datasets for CTC, it is normal to expect a mix of positive (genotoxic/mutagenic) and negative results. The available relevant data on CTC genotoxicity are summarized in two key publications (Manibusan *et al.,* 2007; Eastmond *et al.,* 2008) and the 2005 ATSDR Toxicological Profile for CTC, and the information described here stems mainly from those summary sources. A more recent publication, Uehara *et al.*, 2013, provides supporting data for the later KEs (#4 & 5), which are considered converging KEs, ones which intersect with other AOPs & MOAs, all leading to HCC. While there is some evidence for the later key events for a mutagenic MOA for CTC-induced HCC, for the early, influential key events—which are critical to a determination of a mutagenic MOA-- there are either no data or only sparse supporting data (typically with explanations limiting their relevance), and a significant amount of counterfactual data.

These proposed key events for a mutagenic MOA for CTC are shown schematically in Figure 1-1:

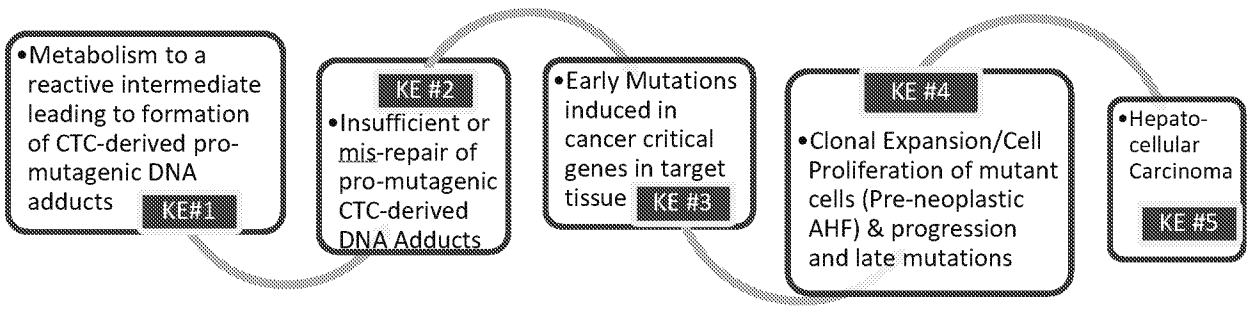

Figure 1-1. Postulated Mutagenic Mode of Action for Carbon Tetrachloride

Carbon tetrachloride (CTC) is metabolized to the highly reactive trichloromethyl free radical by hepatic CYP2E1 metabolism, which can bind macromolecules and lead to: Key Event #1) Formation of pro-mutagenic CTC-derived DNA adducts. This would be followed by Key Event #2) Insufficient or mis-repair of the pro-mutagenic CTC-derived DNA adducts, resulting in Key Event #3) Formation of early mutations induced in cancer critical genes in target tissue, resulting in Key Event #4) Cellular proliferation and clonal expansion to form pre-neoplastic, Altered Hepatic Foci (AHF), along with progression over time (including additional mutations and cell proliferation) to result in Key Event #5) Hepatocellular carcinoma (HCC), the presence of liver tumors.

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A. Qualitative Evaluation of the Weight of Evidence (WOE) for Carbon Tetrachloride (CTC) Acting *via* a Mutagenic MOA (Manibusan *et al.*, 2007; Eastmond *et al.*, 2008; others)

Table 1-1. Qualitatively Evaluate the Comparative Weight of Evidence for Carbon Tetrachloride (CTC) Acting *via* The Mutagenic MOA (Manibusan *et al.*, 2007; Eastmond *et al.*, 2008; others) – (Step 2).

Key Event	Supporting Data	(Potentially) Inconsistent	References
KE#1 Metabolism of CTC to a reactive intermediate that leads to the formation of CTC - induced pro-mutagenic DNA adducts	Use of CYP2E1 knockout mice resulted in no liver histopathological effects, but this is not sufficient to demonstrate essentiality of KE#1 - the formation of CTC-induced pro-mutagenic DNA adducts. There are very limited *in vivo* data to demonstrate DNA binding: either ^{14}C or lipid peroxidation or oxidative adducts, and no data for CTC-derived adducts or Mass Spectrometry support, or evidence of DNA damage, except only in presence of significant cytotoxicity. No CTC–DNA adduct identification has been made, while the polar adducts observed in Syrian hamster liver DNA appear to be derived from lipid peroxidation products (Wang & Liehr, 1995).	Most CTC *in vivo* datasets on DNA binding/DNA damage (36 data sets) are negative or equivocal; DNA adducts are from lipid peroxidation, oxidative adducts, or ^{14}C-binding with no Mass Spectrometry info, thus no data on CTC-induced pro-mutagenic adducts. CTC metabolism resulting in terminal incorporation into cell 1-carbon pool metabolism cannot be ruled out. No ↑ in 8-oxo-dG adducts in liver or in liver mRNA for *Ogg-1*, *Apex*, or *polβ*—all DNA-repair genes (later time points).	**CYP2E1 activating metabolism:** Wong *et al.*, 1998. **Neg strand breaks:** Schwarz *et al.*, 1979; Stewart, 1981;Bermudez *et al.*, 1982; Kitta *et al.*, 1982; Barbin *et al.*, 1983; Brambilla *et al.*, 1983 + **DSB w/ sig hepatotox:** Gans & Korson, 1984; Sasaki *et al.*, 1998; Cabre *et al.*,1999 **Oxidative/lipid peroxidation adducts:** Hadley and Draper, 1990; Chaudhary *et al.*, 1994; Takahashi *et al.*, 1998; Chung *et al.*, 2000; Wacker *et al.*, 2001; Kadiiska *et al.*, 2005; Lopez- Diazguerrero *et al.*, 2005 **Negative genomics and no oxidative DNA adducts**: Uehara *et al.*, 2013 **No CTC-DNA adduct:** Wang & Liehr
KE#2 Insufficient or mis-repair of CTC-induced DNA Adducts	No data available with only two flawed UDS datasets that indicate induction of DNA replication—both associated with significant hepatotoxicity.	Several negative UDS datasets with CTC; ↓ *Polβ* and unchanged *Apex, & Ogg-1* mRNA in liver neonatal mouse model with CTC vs control.	**Negative UDS**: Butterworth *et al.*, 1989; Selden *et al.*, 1994; Craddock and Henderson,1978; Mirsalis & Butterworth, 1980; Mirsalis *et al.*, 1982; Mirsalis, 1987; Madle *et al.*,1994 **Positive (flawed) UDS**: Craddock & Henderson, 1978; Ikegwuonu & Mehendale, 1991 **DNA-repair mRNA:** Uehara *et al.*, 2013
KE#3 Early Mutations induced in cancer critical genes	No gene mutation data in cancer critical genes. Many *in vitro* positive mutation data; but very few *in vivo* positive genetox assays, and they are flawed: MN—only with significant hepatotoxicity)	Three negative *in vivo* transgenic mouse mutation assays; several negative *in vivo* MN/chromo datasets	**Negative TGRAs**: Mirsalis *et al.*, 1994; Tombolan *et al.*, 1999; Hachiya and Motohashi, 2000; Lambert *et al.*, 2005 **Positive (flawed) MN:** Van Goethem *et al.*, 1993, 1995 **Negative MN/Chromo:** Curtis and Tilley, 1968; Sawada *et al.*, 1991; Uryvaeva & Delone, 1995

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Key Event	Supporting Data	(Potentially) Inconsistent	References
KE#4 Clonal Expansion/Cell Proliferation to form Pre-neoplastic AHF with	**40 mkd CTC: regenerative cellular proliferation, ↑ BrdU-cells in peri-portal zone at 24 & 36 hrs; plateauing at 48 hrs.* AHF in high dose mice & rats 13-wk CTC inhalation tox	No data available	Glende *et al.*, 1986; Glende *et al.*, 1992; Lee *et al.*, 1998; Eschen-brenner *et al.*, 1946; Nakata *et al.*, 1975; Doolittle *et al.*, 1987 AHF: Nagano *et al.*, 2007
progression and late mutations	Neonatal mouse: 9-14 wk of 0.2 ml/kg CTC (ip; 2x/wk): liver foci, ↑ BrdU-positive cells; ↑ apoptosis; ↑ oxstress markers: 4-HNE, anisonucleosis, lipofuscin granules		**CTC-induced liver foci, oxidative stress, cell proliferation, apoptosis:** Uehara *et al.*, 2013.
KE#5 Hepatocellular Carcinoma	*Increased incidence of liver tumors in both rats & mice. HCC appears only at the high dose in rats and mid & high doses in mice* In a neonatal mouse model with heightened sensitivity and specificity for tumors: ↑ adenomas & carcinomas in mouse liver w/ CTC were reported.	No data available	Adervont, 1958; Edwards and Dalton, 1942; Edwards *et al.*, 1942; Della *et al.*, 1961; JBRC *et al.*, 1998 **HCC neonatal mouse:** Uehara *et al.*, 2013

**Italicized* entries same as late, converged KEs for CTC cytotoxic/regeneration MOA analysis.

Table 1-2. Incidence of Tumors in F-344 rats and BDF1 mice exposed to carbon tetrachloride vapor for 104 weeks (6hrs/day, 5 days/week). (JBRC *et al.*, 1998)

Tumor	F-344 rats							
	MALE				FEMALE			
	0	5 ppm	25 ppm	125 ppm	**0**	**5 ppm**	**25 ppm**	125 ppm
Adenoma	0/50	1/50	1/50	21/50	0/50	0/50	0/50	40/50
Carcinoma	1/50	0/50	0/50	32/50	0/50	0/50	3/50	15/50
Adenoma or Carcinoma	1/50	1/50	1/50	40/50	0/50	0/50	3/50	44/50
	BDF1 mice							
Adenoma	9/50	9/50	27/50	16/50	2/50	8/49	17/50	5/49
Carcinoma	17/50	12/50	42/50	48/50	2/50	1/49	33/50	48/49
Adenoma or Carcinoma	24/50	20/50	48/50	50/50	4/50	9/49	44/50	48/49

Empirical Support Dose- and Temporal-Concordance:

Most of the available *in vivo* data pertinent to early key events are negative, and cannot support dose-response or temporal concordance for these diagnostic key events for a mutagenic MOA. Later key events, which are converged with other alternative MOAs, have good support because they are consistent with the biological progression for liver tumors.

KE#1 Good supporting data for the initial metabolism step based on the CYP2E1 knock-out mice study demonstrating no liver toxicity, but these data are not sufficient to demonstrate the subsequent formation of pro-mutagenic CTC-derived DNA adducts, which is critical for KE#1. Although DNA binding has been reported for *in vitro* experiments with naked DNA, there is no mass spectrometry-determined demonstration of *in vivo* CTC-derived DNA adducts. The only potential weak *in vivo* support comes from ^{14}C-radiolabeled data that are

ambiguous as to whether they represent adducts or incorporation of radiolabel into normal nucleotides. It is noted that CTC metabolism resulting in incorporation of CTC-derived radiolabeled carbon into cell 1-carbon pool metabolism cannot be ruled out. No CTC–DNA adduct mass spectrometric identification has been made, while the polar adducts observed in Syrian hamster liver DNA appear to be derived from lipid peroxidation products (Wang & Liehr, 1995).

KE#2: Some unreliable, flawed, liver unscheduled DNA synthesis (UDS) positive data are confounded with high hepatotoxicity; several datasets demonstrate *in vivo* negative CTC-liver UDS; Decreased (*Polβ)* or unchanged (*Ogg-1, & Apex)* mRNA (DNA repair-related genes) were quantified in mouse liver with CTC (Uehara *et al.*, 2013).

KE#3: Available *in vivo* evidence is either counterfactual (no increased mutations in 3 *in vivo* transgenic rodent assays) or critically flawed and unreliable due to concurrent high hepatotoxicity.

KE#4: AHF are present in dose-responsive manner (only at two highest exposure levels) after 13-wk exposures to CTC in mice and rats (Nagano *et al.*, 2007). Reasonable support for temporal concordance for effects related to biological progression in CTC-treated mice described in Uehara *et al.,* 2013.

Progression-related events increased with CTC treatment over time (9 wks vs 14 wks): Foci: 0% vs. 12.5%; oxidative damage: 4-HNE; Cell proliferation (BrdU uptake) 15% vs 42%; apoptosis (TUNEL staining).

However, 8-oxodG adducts, which would represent secondary DNA damage (not direct-binding of CTC –derived metabolites to form pro-mutagenic CTC-derived adduct), were not increased by CTC compared to controls, with a non-statistically significant increase in CTC-treated mice at 9 wks which disappeared in the 14-wk treatment group and was described as not increased by the authors (Uehara *et al.*, 2013). Expression of DNA-repair related gene *Polβ* mRNA was lower in CTC-treated 9- and 14-week-old mice compared with controls, while mRNA for *Ogg1* and *Apex* was not changed. <u>These results do not support DNA damage directly from CTC exposure and thus do not support a mutagenic MOA for CTC-induced HCC.</u>

KE#5: Many datasets consistently demonstrate dose-response and temporal concordance for CTC-induced HCC, both within and across studies. Increased incidence of liver tumors was reported in both rats and mice (see Table 2). Hepatocellular carcinomas appear only at the high dose in rats and mid and high doses in mice.

In a neonatal mouse model, with heightened sensitivity, adenomas & carcinomas only appeared at the end of the study, at 22 wks (14 wk of CTC), but were not present at 17 wks (9 wks of CTC), while other early precursor key events occurred before tumor formation, also demonstrating temporal concordance (Uehara *et al.,* 2013).

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Table 1-3. Dose and Temporal Concordance Table

Temporal Concordance →

Dose Concordance ↓

Temporal	<24hrs.	12-36 hrs.	24-72 hrs.	48 hrs.-months	2 yrs. Cancer studies
Dose/Conc.	Metabolism to rxt intermed. Leading to the formation of pro-mutagenic DNA adducts (KE #1)	Insufficient repair or mis- repair of pro- mutagenic DNA adducts (KE#2)	Early induced mutation in cancer critical genes (KE #3)	Cell prolifer'n, clonal expansion of mutant cells, & progression (KE#4)	Hepatocellular carcinoma (HCC) (KE #5)
0 ppm					
5 ppm					
20 ppm				+ (mice)	
25 ppm					++ (mice)
100 ppm				++ (mice)	
125 ppm					+++ (rats & mice)
270/810 ppm^				+++ (rats & mice)	
Mouse*:oral, 1,000; 2,000 Mkd		+/- [UDS-signif. hepatotox or hydroxyurea]			
Hamster, Rat**	[Lipid peroxide-ation/oxidation adducts; **not MS CTC-derived adducts**]				
Rat, Mouse, Hamster***	+/- [^{14}C-DNA binding; no MS]				
Rat MN#			+/- [Surrogate: MN w/ signif. hepatotox]		
Neonatal Mouse&				9 Wks of CTC Liver foci: 0% BrdU+ cells: 15% Adenomas 0% Carcinomas 0% [+ (neonatal mice)]	14 Wks of CTC Liver foci 12.5% BrdU + cells 42% Adenomas 10% Carcinomas 25% [++ (neonatal mice)]

+++ = strong evidence; ++ = moderate evidence; + = weak evidence +/- = equivocal.

^AHF present in mice and rats after 13-wk exposure to CTC at two highest exposures only (270 & 810 ppm): Nagano *et al.,* 2007

* UDS: Craddock & Henderson, 1978; positive attributed to tissue regeneration (not DNA damage); Ikegwuonu & Mehendale, 1991: positive attributed to use of hydroxyurea in experimental design as inadequate DNA replication inhibition.

** Hamster: Wang & Liehr, 1995 (Hamster); Rat: Wacker *et al.,* 2001; Chung *et al.,* 2001; Chaudhary *et al.*, 1994.

***Castro *et al.*, 1989; Animals injected with 770 mg/kg radiolabeled CTC 6 hours before sacrifice; no MS to structurally identify CTC-induced pro-mutagenic adducts (could be 1-C pool incorporation).

#Van Goethem *et al.*, 1993, 1995: MN increase measured during wave of cell proliferation after extensive liver toxicity.

&Uehara *et al.*, 2013: 8-wk mice ip CTC (0.2 ml/kg; 2x/wk; 9 & 14 wk CTC treatment) cell proliferation, oxidative damage at 14 wk; increased foci, cell proliferation, oxidative damage, and liver tumors at 14 wk; decreased *Polβ*, and unchanged *Ogg-1* and *Apex* mRNA in liver at 9 & 14 wks CTC; ~35% liver tumors (adenomas + carcinomas) at 14 wks.

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B. Evolving Bradford Hill Causal Considerations: Qualitative and Quantitative Data Evaluation

Qualitative and quantitative rating categories. [See Becker et al. 2017 for details]

Qualitative	Quantitative	Category description
Strong	3	Multiple studies and/or extensive data provide convincing evidence that the substance causes the KE.
Moderate	2	Some evidence (direct or indirect) indicating the substance causes the KE, but scientific understanding is not yet completely established. There may be some studies that are equivocal.
Weak	1	Very limited evidence (direct or indirect) that the substance causes the KE along this pathway. Scientific understanding of the KE is limited.
No Evidence	0	No data available to support or negate causation of this KE by the substance.
Weak Counter	−1	There is very limited contradictory evidence (direct or indirect) that the substance does not cause this KE.
Moderate Counter	−2	Some evidence (direct or indirect) indicating that the KE is not caused by the substance, but scientific understanding is not completely established. There may be some studies that are equivocal.
Strong Counter	−3	Multiple studies and/or extensive data provide convincing evidence that the substance does not cause this KE.

Biological Plausibility—While the biological plausibility of CTC acting *via* a mutagenic MOA is reasonable, and there are *in vitro* data demonstrating *in vitro* mutagenic activity, there are no supporting *in vivo* data beyond activation of CTC to a reactive metabolite, with substantial counterfactual data to indicate that there is no reliable indication of *in vivo* mutagenicity from CTC.
Qualitative Rating for Biological Plausibility – Strong Counter Evidence for mutagenic MOA (-3)

Essentiality – Essentiality was demonstrated for metabolism and formation of the reactive metabolite by Wong *et al.,* (1998) that showed CTC-induced hepatotoxicity in mice was blocked by using CYP2E1 knockout mice (cyp2e1 -/-); exposure to 1.59 g/kg CTC *via* ip injection resulted in no increase in AST or serum ALT, and an absence of liver histopathology. However, no other reliable data were identified to address Essentiality for a mutagenic MOA for CTC-induced HCC based on influential early key events. No CTC–DNA adduct identification has been made, while the polar adducts observed in Syrian hamster liver DNA appear to be derived from lipid peroxidation products (Wang & Liehr, 1995).

There is some support for essentiality for the later key events, with data showing CTC-induced foci formation can be inhibited by treatment with anti-oxidants (yam) (Chan *et al.,* 2010), which assumes that decreased incidence of foci results in a corresponding decrease in HCC incidence. This is not support for a mutagenic MOA, which relies on the early influential KEs, but could support the link between foci (KE#4) and HCC (KE#5), generally.
Qualitative rating for Essentiality for a Mutagenic MOA: No Evidence (0)

Empirical Support (Dose and Incidence Concordance) - Effects/KEs/Surrogates measured did increase with *in vitro* dose (KEs#1 and 3), but either no evidence or only counter-evidence for *in vivo* effects of early KEs (KE#2: negative UDS or flawed and unreliable positive UDS and no increased mRNA for several DNA-repair genes; KE#3: three negative transgenic *in vivo* mutation assays and several negative MN/CA assays in rodents). Later KEs (#4 & 5) do show dose- response and incidence concordance, but these key events are less informative as they are not specific for a mutagenic MOA, which is largely determined by earlier KEs (#1-3).

KE#1: Metabolism to reactive metabolite leading to the formation of pro-mutagenic CTC-DNA adducts. While the data

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supporting metabolism of CTC *via* CYP2E1 to the trichloromethyl peroxy radical are available, data on subsequent formation of pro-mutagenic CTC-derived adducts are not available. Direct evidence is lacking and the indirect evidence is not convincing. Although there is evidence for *in vitro* binding to naked DNA, appropriate *in vivo* data are lacking. The ^{14}C-DNA binding *in vivo* could be from incorporation of radiolabeled CTC into 1-carbon metabolism; there is no mass spectrometry data to support direct binding of CTC-derived metabolites to DNA to form adducts; the evidence for oxidative damage & peroxidative damage is strong, but does not address CTC-derived pro-mutagenic adducts. In fact, no CTC–DNA adduct identification has been made, while the polar adducts observed in Syrian hamster liver DNA appear to be derived from lipid peroxidation products (Wang & Liehr, 1995). Indeed, most of the DNA damage-related datasets for CTC (36 datasets) are negative or equivocal, providing moderate (but not definitive) counter-evidence.
KE#1 Qualitative Rating – Weak Counter Evidence (-1) for the formation of pro-mutagenic CTC-derived adducts.

KE#2: There are no reliable data to support (the only positive study is an unreliable UDS with significant hepatotoxicity) and some data to refute, with 7 negative UDS datasets; more recently no change or decreased mRNA for 3 DNA repair genes in CTC- exposed (14 wks) mouse liver (Uehara *et al.*, 2013). The neonatal mouse assay has a heightened sensitivity and specificity for tumor response (McClain *et al.,* 2001) and tumors develop rapidly so tumors evident at week 22 are not directly comparable to those reported in traditional 2-year, longer term rodent chronic studies.
KE#2 Qualitative Rating – Moderate Counter Evidence for mutagenic MOA (-2)

KE#3: There are *in vitro* positive datasets to support KE# 3 early induced mutation in cancer critical genes, but no reliable *in vivo* data to support this KE (flawed *in vivo* MN with significant hepatotoxicity), and there are several in *vivo* datasets to counter a mutagenic effect *in vivo* from CTC, with 3 negative transgenic *in vivo* mutation studies (rat & mouse) and several negative *in vivo* chromosomal effect studies (MN and CA).
KE#3 Qualitative Rating – Strong Counter Evidence for mutagenic MOA (-3)

KEs (#4 & #5): These key events are converging ones, at/after intersection points with other alternative MOAs; thus, although strongly supported with empirical data (13-wk CTC AHF (Nagano *et al.*, 2007); sensitive neonatal mouse data (Uehara *et al.*, 2013), these KEs are of lesser importance in the overall determination of a mutagenic MOA.
Qualitative Rating –Moderate (2) for KE#4 & Strong (3) for KE#5 empirical support; but these key events are not exclusive to mutagenic MOA.

<u>Empirical Support (Temporal Concordance)</u>

KE#1: While reactive metabolites must & do occur (substantiated by the CYP2E1 KO lack of liver tumors), the formation of pro-mutagenic DNA adducts has not been demonstrated considering the negative/equivocal DNA damage data. This KE is the starting point for the sequence of KEs for a mutagenic MOA, but there is no definitive *in vivo* evidence of CTC- induced DNA adducts. No CTC–DNA adduct identification has been made, while the polar adducts observed in Syrian hamster liver DNA appear to be derived from lipid peroxidation products (Wang & Liehr, 1995). The mostly negative/equivocal data on DNA damage provides weak counter evidence.
KE#1 Qualitative Rating – Weak Counter Evidence for Mutagenic MOA (-1)

KEs#2 & 3: Very little supportive *in vivo* evidence and substantial *in vivo* counter evidence for both KE#2 (negative UDS; mRNA unchanged/decreased for DNA repair genes) and for influential KE#3, which renders temporal concordance analysis somewhat moot. If indeed CTC operates *via* a mutagenic MOA, then KEs#1-3 must occur early, but *in vivo* evidence for KE#3 includes all counter evidence. Counter evidence from no increased mRNA for DNA repair genes is from later timeframe (14-wk CTC dosing) so does not offer support/counter evidence for temporal concordance.
KE#2 and 3 Qualitative Rating –Moderate Counter Evidence (-2) & Strong Counter Evidence (-3) for KEs#2 & 3 for Mutagenic MOA

KEs#4 &5: These are supported *vis-à-vis* temporal concordance, with cell proliferation increased with increasing duration of treatment; and foci and HCC identified only at study termination, increased cell proliferation at week 9 and increased incidence of liver foci and adenomas and carcinomas at week 14 with the sensitive neonatal mouse model

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(Uehara *et al*., 2013). Presence of AHF without adenoma or carcinoma (Nagano *et al*., 2007) supports temporal sequence of late KEs.

Qualitative Rating –Moderate (2) for KE#4 & Strong (3) for KE#5 empirical support; not exclusive to Mutagenic MOA

Consistency & Analogy

Other haloalkanes are predicted to have the potential to cause cancer, but not necessarily *via* a mutagenic MOA. Indeed, a recent publication on methylene chloride (dichloromethane; DCM)—a close structural analogue to CTC and a mouse liver carcinogen--found no changes in gene expression in any genes related to DNA repair following a 13-wk exposure to mice, even at high (4000 ppm) exposures, a very strong indication that there was no genotoxicity response (Andersen *et al*., 2017). DCM is also metabolized *via* CYP2E1 and, at high doses, *via* GSH-dependent GSTs. Generally many of the haloalkane datasets support non-genotoxic MOAs for HCC, similar to what is proposed for CTC, with a reactive metabolite inducing cytotoxicity leading to cell proliferation, AHF, and eventually liver tumors. As a demonstration of the consistency and analogy criteria being met, most cancer QSAR and predictive models such as the expert system, OncoLogic have a rule that defined haloalkanes with an increased probability of causing liver cancer; however, this modelling approach is hypothesis generating and does not indicate empirical support for any particular cancer MOA.

Qualitative Rating – Moderate Counter Evidence (-2) (KEs#1 & 2); Strong Counter Evidence (-3) for mutagenic MOA (KE#3); Strong (3) (KEs# 4 & 5).

C. Qualitative and Quantitative Rating of the Key Events for Bradford Hill Causal Considerations

Table 1-4. Qualitative Rating of the Key Events for Bradford Hill Causal Considerations (Step 3).

Bradford Hill Causal Considerations	Key Event #1	Key Event #2	Key Event #3	Key Event #4	Key Event #5
	Metabolism to rxt intermed. & Formation of pro-mutagenic DNA adducts (KE#1)	Insufficient repair or mis-repair of pro-mutagenic DNA adducts (KE #2)	Early induced mutation in cancer critical genes (KE #3)	Cell prolifer'n, clonal expansion of mutant cells, & progression (KE #4)	Hepatocellular carcinoma (HCC) (AO) (KE#5)
Biological Plausibility	Not scored for the case example, but extant data demonstrates not biologically plausible – strong counter (-3)				
Essentiality	No evidence* (0)	No evidence (0)	No evidence (0)	No evidence (0)	No evidence (0)
Empirical Support – Dose and Incidence Concordance	Weak counter evidence (-1)	Moderate counter (-2)	Strong counter (-3)	Moderate (+2)	Strong (+3)
Empirical Support – Temporal Concordance	Weak counter (-1)	Moderate counter (-2)	Strong counter (-3)	Moderate (+2)	Strong (+3)
Consistency & Analogy	Moderate counter (- 2)	Moderate counter (-2)	Strong counter (-3)	Strong (+3)	Strong (+3)

***No evidence of CTC-specific pro-mutagenic DNA adducts**

Considerations & Challenges for CTC MOA quantitative analysis:

CTC presents special challenges in quantitative analysis for a mutagenic MOA because the influential KEs are the early ones related to an early induction of a mutation in critical genes, represented by KE#1, 2, and 3.

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The later KEs, 4 & 5, represent converging KEs, ones that are common to other alternative MOAs; they are not informative for a decision on whether a mutagenic MOA is operating or not. This is addressed in part by applying an adjustment factor (10%) to the quantitative weighting of the later KEs (see Table 1-5).

Overall, based on the available data, quantitative scoring for confidence in a mutagenic MOA for CTC induction of liver tumors indicates this MOA is not very probable for CTC. A confidence score of -36 clearly indicates that a mutagenic MOA is not supported by the available data on CTC-induced HCC.

D. Composite Quantification of the WOE for a Mutagenic MOA

Table 1-5. Composite Quantification of the WOE for the Mutagenic MOA (Step 4 and 5).

Bradford Hill Causal Considerations	Key Event #1	Key Event #2	Key Event #3	Key Event #4	Key Event #5
	Metabolism to rxt intermed. & Formation of pro-mutagenic DNA adducts (KE#1)	Insufficient repair or mis-repair of pro- mutagenic DNA adducts (KE #2)	Early induced mutation in cancer critical genes (KE #3)	Cell prolifer'n, clonal expansion of mutant cells, & progression (KE #4) AF: 0.1*	Hepatocellular carcinoma (HCC) (KE#5) AF: 0.1
Essentiality (40%)	0*	0	0	0	0
Empirical Support – (20%) Dose and Incidence Concordance	-0.2	-0.4	-0.6	+0.4	+0.6
Empirical Support – (20%) Temporal Concordance	-0.2	-0.4	-0.6	+0.4	+0.6
Consistency (10%)	-0.2	-0.2	-0.3	+0.2	+0.3
Analogy (10%)	-0.2	-0.2	-0.3	+0.3	+0.3
KE TOTALs Sum = -3.51	-0.8	-1.2	-1.8	+0.13 (1.3 x 0.1)	+0.18 (1.8 x 0.1)

***No evidence of CTC-specific pro-mutagenic DNA adducts.**

MOA Confidence Score = -3.51/9.6 (x 100) = - 36.35

*Adjustment Factor of 10% (0.1) applied to late key events due to convergence and lack of specificity to a particular MOA.

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E. Key References

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IV. Evaluating the WOE for a Cytotoxic MOA

There is considerable *in vivo* and *in vitro* scientific evidence supporting the mode of action by which carbon tetrachloride produces toxic effects in animals. Mechanistic studies support the following key events in the carcinogenicity of carbon tetrachloride: (KE1) metabolism to trichloromethyl radical by CYP2E1 and subsequent formation of trichloromethyl peroxy radical; (KE2) autocatalytic lipid peroxidation due to the attack on the cellular membrane by the trichloromethyl peroxy radical; (KE3) loss of calcium homeostasis leading to activation of degenerative enzymes and cytotoxicity; (KE4) if exposures above the threshold for hepatotoxicity continue, sustained regenerative and proliferative changes in the liver persist which increases the rate of stem cell division, thereby increasing the probability of fixation of background DNA damage as mutations and an increase in the number of intermediate cell populations that can progress to malignancy; and an increase in cancer incidence (KE#5) (Manibusan et al. 2007, Eastmond, 2008; Borgert et al., 2015).

Provided below is the postulated mode of action in Figure 2-1.

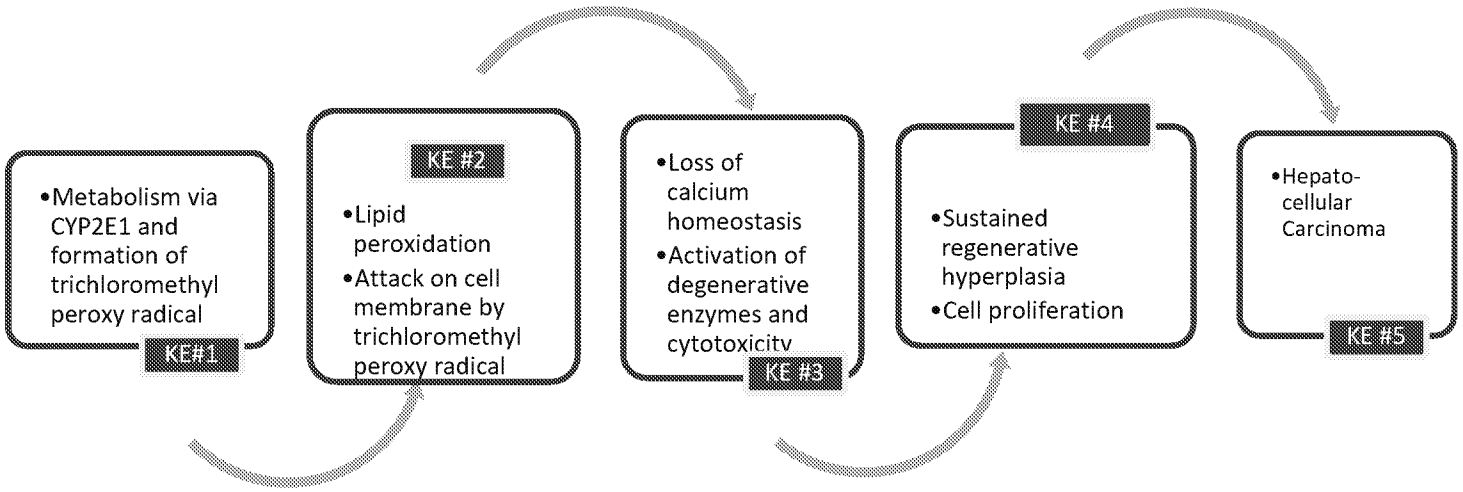

Figure 2-1. Postulated Non-Genotoxic, Cytotoxic Mode of Action for Carbon Tetrachloride.

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A. Qualitative Evaluation of the Weight of Evidence (WOE) for Carbon Tetrachloride Acting via a Cytotoxic MOA

Table 2-1. Qualitatively Evaluate the Comparative Weight of Evidence (WOE) for Carbon Tetrachloride Acting via a Cytotoxic MOA (Manibusan et al., 2007; Eastmond, 2008).

Key Event	Supporting Data	Potentially Inconsistent	References
Metabolism via CYP2E1 and formation of Trichloromethyl peroxy radical (KE#1)	Available spin-trapping studies on free-radical products formed by metabolic activation of carbon tetrachloride in rat liver microsomes and *in vivo* in the rat (Albano et al., 1982). Recent studies by Poyer et al. (1980) and Tomasi et al., (1980) have reported successful trapping of CCL3• in liver microsomal fractions with spin trap N-benzylidene-2-methylpropyl-amine N-oxide (PBN). Experiments with PBN give unequivocal proof that CCL3• is produced in isolated liver cells or in liver microsomes exposed to CTC. Studies using CYP450 inhibitors have shown that inhibition of carbon tetrachloride metabolism prevents subsequent liver induced damage. CYP2E1 knockout mice resulted in no liver histopathological effects.	No data available	Poyer et al., 1980 Albano et al., 1982 Tomasi et al., 1980 Martinez et al., 1995; Letteron et al., 1990; Mourelle et al., 1988; Bechtold et al., 1982; Weddle et al., 1976; Wong et al., 1998; Takahashi et al., 2002
Lipid Peroxidation and attack of cellular membranes (KE #2)	Studies of radical scavengers that are not necessarily specific to trichloromethyl peroxy or lipid peroxidative free radicals have shown that these agents confer protection against carbon tetrachloride induced liver toxicity, while another study demonstrated administration of α-tocopherol, Vitamin E antioxidant, had been shown to reduce lipid peroxidation (Gee et al., 1981). Numerous studies have demonstrated lipid peroxidation following carbon tetrachloride exposure by the detection of conjugated dienes in liver lipids, increased exhalation of ethane and pentane (end degradation products of peroxidized polyunsaturated fatty acids) or malondialdehyde and 4-HNE. Hartley et al., (1999) demonstrated the temporal relationship between carbon tetrachloride exposure initiated lipid peroxidation, liver damage and formation of 4-HNE and MDA protein adducts.	No data available	Azri et al., 1991; Gordis et al., 1969; Slater et al., 1981; Packer et al., 1978; Comporti et al., 1985; Gee et al., 1981. Comporti et al., 1984; Lee et al., 1982; Younes et al., 1985; Gee et al., 1981; deZwart et al., 1997; Ichinose et al., 1994; Hartley et al., 1999; Cabre et al., 2000
Loss of calcium homeostasis and initiation of cytotoxicity (KE #3)	Studies have reported 100-fold or more increases in cytosolic concentrations of calcium following exposure to carbon tetrachloride. Studies have demonstrated that effect of carbon tetrachloride on membrane integrity and the active transport that	No data available	Agarwal et al., 1986; Agarwal et al., 1984; Long et al., 1986; Kroner et al., 1982; Lowrey et al., 1981; Moore et al., 1980; Moore et al., 1976;

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Key Event	Supporting Data	Potentially Inconsistent	References
	may be by the NADPH-cytochrome P-450 electron-transport chain in liver endoplasmic reticulum, a distance away from the nucleus (Slater, 1972; Recknagel et al., 1977; McCay, 1980), which appear to be secondary to lipid peroxidation.		Hemmings et al., 2002; Racay et al., 1997; Gubskii et al., 1990; Limaye et al., 2003; Slater, 1972; Recknagel et al., 1977 and McCay, 1980
Sustained regenerative cellular proliferation (KE #4)	Administration of 40 mg/kg carbon tetrachloride induced sustained regenerative cellular proliferation, as measured by the increase in BrdU-positive cells in the peri-portal zone at 24 hrs. increasing at 36 hrs. and plateauing at 48 hrs. AHF after 13-wk, only at highest doses	No data available	Glende et al., 1986; Glende et al., 1992; Lee et al., 1998; Eschenbrenner et al., 1946 Nakata et al., 1975; Doolittle et al., 1987 Nagano *et al.*, 2007
Liver tumors (KE #5)	Increased incidence of liver tumors in both rats and mice (see Table 2- 2). Hepatocellular carcinomas appear only at the high dose in rats and mid and high doses in mice, with an all or none response.	No data available	Adervont, 1958; Edwards and Dalton, 1942 Edwards et al., 1942; Della et al., 1961; JBRC et al., 1998

Table 2-2. Incidence of Tumors in F-344 rats and BDF1 mice exposed to carbon tetrachloride vapor for 104 weeks (6hrs/day, 5 days/week). (JBRC et al., 1998)

Tumor	F-344 rats							
	MALE				FEMALE			
	0	5	25	125	0	5	25	125
Adenoma	0/50	1/50	1/50	21/50	0/50	0/50	0/50	40/50
Carcinoma	1/50	0/50	0/50	32/50	0/50	0/50	3/50	15/50
Adenoma or Carcinoma	1/50	1/50	1/50	40.50	0/50	0/50	3/50	44/50
	BDF1 mice							
Adenoma	9/50	9/50	27/50	16/50	2/50	8/49	17/50	5/49
Carcinoma	17/50	12/50	42/50	48/50	2/50	1/49	33/50	48/49
Adenoma or Carcinoma	24/50	20/50	48/50	50/50	4/50	9/49	44/50	48/49

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Table 2-3. Dose and Temporal Concordance Table.

Temporal Concordance →

Dose Concordance ↓

Temporal	<24hrs.	12-36 hrs.	24hrs	48 hrs. +	2 yrs. Cancer studies
Dose/Conc.	Metabolism to Trichloromethyl Peroxy Radical (KE #1)	Lipid peroxidation and attack on cellular membranes (KE #2)	Loss of calcium homeostasis and initiate cytotoxicity (KE #3)	Sustained regenerative cellular proliferation, hyperplasia (KE #4)	Liver tumors (KE #5) – 2 year cancer studies in mice and rats
800 µL/100 g	+ (rats) based on spin-trapping studies				
5 ppm					
20 ppm		+ (mice)		+ (mice)	
25 ppm					+ (mice)
100 ppm		+ (rats)		++ (mice)	
125 ppm					++ (rats & mice)
270/810 ppm				++ (mice & rats)	
1.59 g/kg	+	+			
50 uM			+		

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B. Evolving Bradford Hill Causal Considerations: Qualitative and Quantitative Data Evaluation

Qualitative and quantitative rating categories. [See Becker et al. 2017 for details]

Qualitative	Quantitative	Category description
Strong	3	Multiple studies and/or extensive data provide convincing evidence that the substance causes the KE.
Moderate	2	Some evidence (direct or indirect) indicating the substance causes the KE, but scientific understanding is not yet completely established. There may be some studies that are equivocal.
Weak	1	Very limited evidence (direct or indirect) that the substance causes the KE along this pathway. Scientific understanding of the KE is limited.
No Evidence	0	No data available to support or negate causation of this KE by the substance.
Weak Counter	−1	There is very limited contradictory evidence (direct or indirect) that the substance does not cause this KE.
Moderate Counter	−2	Some evidence (direct or indirect) indicating that the KE is not caused by the substance, but scientific understanding is not completely established. There may be some studies that are equivocal.
Strong Counter	−3	Multiple studies and/or extensive data provide convincing evidence that the substance does not cause this KE.

Essentiality – For key event #1, there is a study by Wong et al., (1998) that demonstrated carbon tetrachloride-induced hepatotoxicity in mice using CYP2E1 knockout mice (cyp2e1 -/-) exposed to 1.59 g/kg carbon tetrachloride via intraperitoneal injection resulted in no increase in AST or serum ALT liver enzyme activity, and an absence of corresponding liver histopathological effects. Conversely, hepatocyte cell lines that over-express cytochrome P450 have increased levels of carbon tetrachloride-induced cytotoxicity. (Jaeschke et al., 2002; Takahashi et al., 2002 and Dai and Cederbaum, 1995).

Qualitative Rating – Strong (3)

Empirical Support (Dose and Incidence Concordance) - Because the earlier key events are demonstrated via *in vitro* assays, the concentrations do not align with the longer term *in vivo* studies. It is clear, however, that the doses for the earlier key events are lower than those needed to elicit liver tumors, which is what you expect to demonstrate for dose concordance that the precursor key events must occur earlier and at lower doses than the tumorigenic dose. The increased incidence of rodent liver tumors is limited to the highest dose tested, a clear threshold type of response (Table 2). Exposure to carbon tetrachloride elicits AHF at 13-wk at high exposures (270 and 810 ppm only), with no tumors, and tumors at doses between 25 ppm in the carcinogenic mouse study and 125 ppm in the chronic/carcinogenicity study in the rat. Data demonstrating dose concordance is moderate to strong, which is based on the good alignment of earlier key events to the tumorigenic dose.

Qualitative Rating – Moderate (2)

Empirical Support (Temporal Concordance) – Cabre et al. (2000) demonstrated temporal concordance between liver lipid peroxidation, glutathione metabolism and development of liver cirrhosis in male Wistar rats exposed to 0.5mL carbon tetrachloride via IP for a total of 9 week, which may be considered a high dose exposure that is relevant to establish empirical support for the cytotoxic key events. By the second week, all livers were fibrotic, and cirrhosis appeared in all treated animals by week 9. Glutathione levels were reduced beginning at week 5 and glutathione peroxidase activity was significantly decreased at week 7 in carbon tetrachloride treated rats. Lipid peroxide-derived aldehydes were elevated starting at week 7. Effects of carbon tetrachloride on cell membrane

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integrity and active transport system appear to be secondary (temporally) to lipid peroxidation. Preincubation of liver microsomes with membrane soluble antioxidants protected against the loss of calcium from microsomes and the loss of calcium ATPase activity in a dose- dependent manner. Authors conclude that lipid peroxidation impairs sequestration of calcium ions in microsomes by increasing microsomal membrane permeability and interfering with enzyme activity by altering lipid-calcium pump interactions. Data supporting temporal concordance is considered strong as the data demonstrate lipid peroxidation occurs before loss of calcium occurs and subsequent cell proliferation.

Qualitative Rating – Strong (3)

Consistency and Analogy – Other structurally similar haloalkanes have demonstrated the ability to elicit rodent liver tumors via a nongenotoxic, cytotoxic mode of action; this mode of action typically involves formation of a more reactive metabolite or toxic moiety that causes cell membrane damage, or cytotoxic effects that may lead to sustained regenerative cell hyperplasia and formation of preneoplastic lesions leading to late forming, liver tumors at high doses of exposure. As further demonstration of the consistency and analogy criteria being met, most cancer QSAR and predictive models such as OncoLogic has a rule the defined haloalkanes with an increased probability of causing liver cancer without specifying the mode of action.

Qualitative Rating – Strong (3)

C. Qualitative and Quantitative Rating of the Key Events for Bradford Hill Causal Considerations.

Table 2-4. Qualitative Rating of the Key Events for Bradford Hill Causal Considerations.

Bradford Hill Causal Considerations	Key Event #1	Key Event #2	Key Event #3	Key Event #4	Key Event #5
	Metabolism to Trichloromethyl Peroxy Radical	Lipid Peroxidation and attack on cellular membranes	Loss of calcium homeostasis and initiate cytotoxicity	Sustained regenerative cellular proliferation, hyperplasia	Liver tumors
Essentiality	Strong (+3)	Strong(+3)	Strong(+3)	Strong (+3)	Strong (+3)
Empirical Support – Dose and Incidence Concordance	Moderate (+2)	Moderate (+2)	Moderate (+2)	Moderate (+2)	Strong (+3)
Empirical Support – Temporal Concordance	Strong (+3)	Strong (+3)	Strong (+3)	Strong (+3)	Strong (+3)
Consistency	Strong (+3)	Strong (+3)	Strong (+3)	Strong (+3)	Strong (+3)
Analogy	Strong (+3)	No evidence (0)	No evidence (0)	Strong (+3)	Strong (+3)

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D. Composite Quantification of the WOE for a Cytotoxic MOA

Table 2-5 Quantification of the WOE for the Cytotoxic MOA.

Bradford Hill Causal Considerations	Key Event #1	Key Event #2	Key Event #3	Key Event #4	Key Event #5
	Metabolism to Trichloromethyl Peroxy Radical	Lipid Peroxidation and attack on cellular membranes	Loss of calcium homeostasis and initiate cytotoxicity	Sustained regenerative cellular proliferation, Hyperplasia*	Liver tumors*
Essentiality (40%)	1.2	1.2	1.2	1.2	1.2
Empirical Support – (20%) Dose and Incidence Concordance	0.4	0.4	0.4	0.4	0.6
Empirical Support – (20%) Temporal Concordance	0.6	0.6	0.6	0.6	0.6
Consistency (10%)	0.3	0.3	0.3	0.3	0.3
Analogy (10%)	0.3	0	0	0.3	0.3
KE TOTALs Sum = 8.38	2.8	2.5	2.5	0.28 (2.8 x 0.1)	0.3 (3 x 0.1)

Mode of Action Confidence Score = 8.38/9.6 = 87

*Adjustment Factor of 10% (0.1) applied to late key events due to convergence and lack of specificity to a particular MOA.

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D. Key References

Borgert CJ, Wise K, Becker RA. 2015. Modernizing problem formulation for risk assessment necessitates articulation of mode of action Regul Toxicol Pharmacol. 2015 Aug; 72(3):538-51. doi: 10.1016/j.yrtph.2015.04.018. Epub 2015 Apr 27.

Eastmond DA. 2008. Evaluating genotoxicity data to identify a mode of action and its application in estimating cancer risk at low doses: A case study involving carbon tetrachloride Environ Mol Mutagen. Mar; 49(2):132-41. doi: 10.1002/em.20368.

Manibusan MK, Odin M, Eastmond DA. 2007. Postulated carbon tetrachloride mode of action: a review. J Environ Sci Health C Environ Carcinog Ecotoxicol Rev. Jul-Sep; 25(3):185-209.

V. Conclusions

Two hypothesized MOAs were evaluated for liver tumors induced in rodents by carbon tetrachloride using the quantitative MOA confidence scoring method described by Becker et al., 2017. This method provides a means to compare the WOE for the default MOA (induction of rodent liver tumors *via* a mutagenic MOA) to the WOE for a cytotoxicity and sustained regenerative cellular proliferation MOA.

The confidence scoring results indicate it is highly unlikely that a mutagenic mode of action is plausible for carbon tetrachloride-induced rodent liver tumors. Based on the MOA confidence score of -36, the weight of evidence clearly does not support a mutagenic mode of action for carbon tetrachloride. The negative score indicates there is strong counter evidence for several of the early, diagnostic, KEs for a mutagenic MOA. In other words, the available data indicate that it is highly unlikely that rodent liver tumors are induced by carbon tetrachloride via a mutagenic mode of action.

In contrast, there are significant mechanistic data to support a non-linear, non-genotoxic mode of action for carbon tetrachloride. Based on the MOA confidence score of +87, the weight of evidence clearly supports a cytotoxic mode of action for carbon tetrachloride induction of rodent liver tumors. The MOA causal confidence scoring results indicate that the more likely operative MOA is cytotoxicity and sustained regenerative cellular proliferation. Therefore, an increase in cancer risk would only occur at doses that exceed a specific threshold.

The overall pattern of observations is very consistent with a non-linear, threshold mode of carcinogenic action, as evident by the MOA confidence score of +87 for cytotoxicity compared to the mutagenic MOA score of -36. Therefore, it would be inappropriate to use a linear default for extrapolating cancer risks. Instead, the causal weight of the scientific evidence analysis supports use of a threshold, non-linear method for determining potential cancer risks.

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VI. Appendix A. Quantitative Weight of Evidence to Assess Confidence in Potential Modes of Action (Becker et al., 2017)

Quantitative weight of evidence to assess confidence in potential modes of action

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Regul Toxicol Pharmacol. 86: 205-220, 2017.

Full article can be downloaded at: http://www.sciencedirect.com/science/article/pii/S0273230017300387?via%3Dihub

ABSTRACT: The evolved World Health Organization/International Programme on Chemical Safety mode of action (MOA) framework provides a structure for evaluating evidence in pathways of causally linked key events (KE) leading to adverse health effects. Although employed globally, variability in use of the MOA framework has led to different interpretations of the sufficiency of evidence in support of hypothesized MOAs. A proof of concept extension of the MOA framework is proposed for scoring confidence in the supporting data to improve scientific justification for MOA use in characterizing hazards and selecting dose-response extrapolation methods for specific chemicals. This involves selecting hypothesized MOAs, and then, for each MOA, scoring the weight of evidence (WOE) in support of causality for each KE using evolved Bradford Hill causal considerations (biological plausibility, essentiality, dose-response concordance, consistency, and analogy). This early proof of concept method is demonstrated by comparing two potential MOAs (mutagenicity and peroxisome proliferator activated receptor-alpha) for clofibrate, a rodent liver carcinogen. Quantitative confidence scoring of hypothesized MOAs is shown to be useful in characterizing the likely operative MOA. To guide method refinement and future confidence scoring for a spectrum of MOAs, areas warranting further focus and lessons learned, including the need to incorporate a narrative discussion of the weights used in the evaluation and an overall evaluation of the plausibility of the outcome, are presented.

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EARTHJUSTICE * ALASKA COMMUNITY ACTION ON TOXICS * ENVIRONMENTAL HEALTH STRATEGY CENTER * ENVIRONMENTAL WORKING GROUP * LEARNING DISABILITIES ASSOCIATION OF AMERICA * SIERRA CLUB * UNION OF CONCERNED SCIENTISTS * UNITED STEEL, PAPER AND FORESTRY, RUBBER, MANUFACTURING, ENERGY, ALLIED INDUSTRIAL AND SERVICE WORKERS INTERNATIONAL UNION, AFL-CIO/CLC * WE ACT FOR ENVIRONMENTAL JUSTICE

Submitted online via *Regulations.gov* to dockets EPA–HQ–OPPT–2016–0736, EPA–HQ–OPPT–2016–0741, EPA–HQ–OPPT–2016–0723, EPA–HQ–OPPT–2016–0733, EPA–HQ–OPPT–2016–0735, EPA–HQ–OPPT–2016–0742, EPA–HQ–OPPT–2016–0743, EPA–HQ–OPPT–2016–0725, EPA–HQ–OPPT–2016–0732 and EPA–HQ–OPPT–2016–0737

Earthjustice, Alaska Community Action on Toxics, Environmental Health Strategy Center, Environmental Working Group, Learning Disabilities Association of America, Sierra Club, Union of Concerned Scientists, United Steel, Paper and Forestry, Rubber, Manufacturing, Energy, Allied Industrial and Service Workers International Union, AFL-CIO/CLC, and WE ACT for Environmental Justice — Petitioners and counsel for Petitioners in *Safer Chemicals, Healthy Families v. US EPA*, No 17-72260 (9th Cir.) — submit these comments in strong opposition to many of the approaches taken by the United States Environmental Protection Agency (EPA) in the Problem Formulations of the Risk Evaluations for the "first ten chemicals": asbestos, 1-bromopropane, carbon tetrachloride, 1, 4-dioxane, cyclic aliphatic bromide cluster (HBCD), methylene chloride, N-methylpyrrolidone, perchloroethylene, pigment violet 29, and trichloroethylene (together, problem formulations). We also oppose EPA's reliance, in the risk evaluation process for these chemicals, on its "Application of Systematic Review in TSCA Risk Evaluations" document (TSCA systematic review protocol),[1] which will likely result in the

[1] US EPA, *Application of Systematic Review in TSCA Risk Evaluations* EPA Document# 740-P1-8001 (2018).

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exclusion of meaningful information from EPA's risk evaluations in violation of TSCA section 26. If EPA continues to follow the approach it has laid out in the problem formulations, it will leave the public—and especially vulnerable groups like children, pregnant women, and workers—at ongoing unreasonable risk from the first ten chemicals that are being evaluated under the Toxic Substances Control Act (TSCA). These comments lay out how the problem formulations and TSCA systematic review protocol fail to comply with the language, intent, and purpose of TSCA.

Introduction

Many of the flaws with the problem formulations reflect applications of the illegal processes laid out in Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act, 82 Fed. Reg. 33,726 (July 20, 2017), codified at 40 C.F.R. § 702.31 through § 702.51 ("Risk Evaluation Rule"). Our organizations have challenged the Risk Evaluation Rule, and this suit is pending before the U.S. Court of Appeals for the Ninth Circuit.[2] If the Ninth Circuit rules that the Risk Evaluation Rule is illegal in any manner that implicates processes, reasoning, or methodologies used in developing the problem formulations, EPA will have to revise the risk evaluations of the first ten chemicals to bring them into compliance with TSCA.

The overriding flaw in the problem formulations is that EPA is not taking a holistic approach to assessing risk, as TSCA mandates. Rather, EPA is excluding from its risk evaluations: hazards; exposure pathways; consideration of the impact of chemicals on vulnerable populations that were identified in the scopes of the risk evaluations of the first ten chemicals published in July 2017; and known or reasonably foreseen conditions of use. It is also

[2] *Safer Chemicals, Healthy Families v. US EPA*, No. 17-72260 (9th Cir. filed Aug. 10, 2017).

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adopting an impermissibly narrow view of the term "conditions of use," such that it excludes ongoing use and disposal of chemicals that are no longer manufactured for that use -- what EPA terms "legacy use" and "associated disposal" -- and ongoing exposures from disposals that initially occurred in the past (what EPA calls "legacy disposal"). Given this panoply of exclusions, the risk evaluations will not accurately characterize the true risk posed by "the chemical substance" under "the conditions of use," as required by TSCA section 6(b)(4).

Congress enacted TSCA in 1976 to give EPA authority to "look comprehensively at the hazards associated with [a] chemical" and to prevent harm to health and the environment through regulation of chemicals posing unreasonable risks. S. Rep. No. 94-698, at 2 (1976). While other federal environmental laws focus on specific media, such as air or water, before TSCA was adopted no federal law gave EPA authority to "look comprehensively" at the hazards of a chemical "in total." *Id.* Congress designed TSCA to fill these "regulatory gaps," S. Rep. No. 94-698, at 1, by adopting 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. This comprehensive approach is needed because individuals are often exposed to a chemical from multiple uses through a variety of exposure pathways. TSCA can effectively protect against chemical harm only if EPA evaluates *all hazards and all exposures* to a chemical substance. If EPA does not fully consider all known and reasonably foreseen hazards and exposures during a risk evaluation, the evaluation cannot accurately characterize the true risk posed by the chemical. If EPA fails to accurately characterize risk, it cannot identify and meaningfully manage unreasonable risks.

In addition to improper exclusions, the problem formulations are flawed by failure to rely on "information . . . that is reasonably available to the Administrator," within the meaning of

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TSCA,[3] which EPA defines as "information that EPA possesses *or can reasonably generate, obtain and synthesize for use*" in the relevant timeframe.[4] Defying this requirement, many of the proposed exclusions from the risk evaluations are based on inappropriate conjecture and/or incomplete, ambiguous, and self-serving reports by a subset of manufacturers and processors to the effect that they have ceased manufacture. EPA should not rely on such representations because they may not provide complete information. Moreover, a decision to cease manufacture could be reversed at any time, and such resumption may be "reasonably foreseen." EPA must ascertain whether resumption of discontinued uses is reasonably foreseeable. Excluding conditions of use from risk evaluations based on a manufacturer's report that the chemical was discontinued will invite attempts to "game" the process. Even if, upon analysis of all reasonably available information, EPA concludes that re-commencement is not reasonably foreseen, it should not exclude discontinued conditions of use from final risk evaluations unless it also adopts a SNUR that ensures that EPA will receive notice and the opportunity to review -- and deny -- a proposal to re-commence manufacture for conditions of use that are not included in TSCA section 6(b) risk evaluations.

We urge EPA to revise its illegal approaches now, rather than waiting for a federal court to order the agency to make such revisions. Continuing down the current path, which will inevitably need to be revised to bring it in line with the plain meaning of TSCA, will only delay the process and jeopardize EPA's compliance with the timelines mandated by Congress.

A. The problem formulations violate TSCA by excluding known or reasonably foreseen "conditions of use" and "exposure pathways" of the first ten chemicals

[3] 15 U.S.C. § 2625(k).

[4] 40 C.F.R. § 702.3 (emphasis added).

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In conducting a TSCA section 6(b) risk evaluation, EPA must "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other nonrisk factors … under the conditions of use."[5] The directive to "determine whether *a chemical substance* presents an unreasonable risk" requires an evaluation of the chemical's total risk. And the phrase "under *the* conditions of use" unambiguously means *all* of the chemical's conditions of use. That EPA lacks the authority to pick and choose which conditions of use it includes in its TSCA section 6(b) risk evaluations is discussed in detail at pages 21-38 of Petitioners' Opening Brief in *Safer Chemicals, Healthy Families v. U.S. EPA*, No. 17-72260 (9th Cir. filed Apr. 16, 2018) ("Petitioners' Opening Brief"), a copy of which is attached hereto as Exhibit 1, and incorporated herein by reference.

A non-exhaustive sampling of the illegal exclusions proposed in the problem formulations follow.

1. Consumer product exclusions

The problem formulations indicate that EPA plans to exclude from its first ten risk evaluations exposures to chemicals resulting from their known presence in consumer products based on EPA's assertion that their presence is unintended or *de minimis*. These exclusions are not permitted. As one example, EPA plans to exclude consideration of exposure to 1,4-dioxane (a likely human carcinogen) when it is present in consumer products, such as detergents. EPA acknowledges that 1,4-dioxane is present in consumer products, but argues that it is present as a byproduct and that "contamination" is not an "intended" condition of use.[6] Similarly, EPA plans to exclude consideration of exposure to HBCD from its use in children's products, such as toys

[5] 15 U.S.C. § 2605(b)(4)(A).

[6] US EPA, *Problem Formulation of the Risk Evaluation for 1,4-Dioxane*, 18 (2018).

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and car seats, even though manufacturers reported to Washington State Department of Ecology (WSDE) that certain toys and car seats contained HBCD, and independent testing by WSDE confirmed the presence of HBCD in some products.[7] EPA's theory for exclusion is that HBCD was not intentionally added to these products as a flame retardant.

As explained more fully in Petitioners' Opening Brief, EPA's rationales for excluding these consumer exposures to 1,4-dioxane and HBCD are inconsistent with TSCA. These substances are "known" and/or "reasonably foreseen" to be present in consumer products, irrespective of whether they are "intended" to be there. The known and foreseeable presence of these substances in consumer products are "conditions of use" within the meaning of TSCA section 2(4) insofar as they are "circumstances . . . under which [the] chemical substance is . . . known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of."[8] Under the statutory definition of "condition of use," it is irrelevant whether a chemical is present in a product unintentionally.

Additionally, EPA plans to exclude exposure to carbon tetrachloride (a probable human carcinogen) from sealants, adhesives, and arts and crafts products because it claims such uses present "de minimis exposure."[9] EPA may not exclude "de minimis" exposures from a risk evaluation because there is no way for EPA to determine which conditions of use will result in de minimis exposure or risk *before* conducting the evaluation whose very purpose is to assess the exposures and risks from those conditions of use. In other words, the risk evaluation is the

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[7] US EPA, *Problem Formulation for Cyclic Aliphatic Bromides Cluster*, 23-24 (2018). EPA also proposed to exclude ongoing uses of HBCD in commercial textiles simply on the basis that the use "appeared to be phasing out." *Id.* at 22. TSCA does not permit this.

[8] 15 U.S.C. § 2602(4).

[9] US EPA, *Problem Formulation of the Risk Evaluation for Carbon Tetrachloride,* 21 (2018).

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process that allows EPA to determine what levels of exposure to a given chemical are insignificant or de minimis. Any attempt to establish a de minimis level of exposure before completion of the risk evaluation would put the cart before the horse; EPA cannot know what is de minimis until it has completed its evaluation. Indeed, the problem formulation demonstrates just this problem. EPA has identified a set of exposures it deems de minimis, but there is no analysis of the actual exposures or the risk such exposures present. That analysis should be part of the risk evaluation that EPA is developing. Moreover, TSCA requires EPA to conduct risk evaluations that consider risks from multiple (sometimes relatively low-dose) exposures to the same chemical. EPA's proposal to exclude conditions of use that result in low exposures would prevent EPA from accurately evaluating total risks to vulnerable subpopulations like children, for whom low doses can pose significant risks, especially when they add up. *See Petitioners' Opening Brief*, at 37-38.

2. Environmental statute exclusions

Each of the problem formulations indicates that EPA plans to exclude exposure pathways on the grounds that such exposures are, or might someday be, regulated in some way under other environmental statutes (though not necessarily under a risk-based safety standard that excludes consideration of costs, as mandated by TSCA) under other environmental statutes.[10] Applying this new exclusion, which was not identified in the scopes of the first ten chemicals, EPA plans

[10] *See, e.g.*, US EPA, *Problem Formulation of the Risk Evaluation for Carbon Tetrachloride*, at 13; US EPA, *Problem Formulation for Cyclic Aliphatic Bromides Cluster*, at 13; US EPA, *Problem Formulation of the Risk Evaluation for 1,4-Dioxane*, at 37; US EPA, *Problem Formulation of the Risk Evaluation for 1-Bromopropane*, at 13. Each of these documents states that EPA will exclude 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).

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to exclude consideration of many well-known exposures of concern. This approach is antithetical to the statutory language, structure and purpose of TSCA, which requires EPA to evaluate chemicals under TSCA holistically and comprehensively. *See Petitioners' Opening Brief*, at 21-38.

For example, even though carbon tetrachloride is listed as a hazardous air pollutant under the CAA, emissions standards apply only to a limited list of industrial sources, and the emissions standards are based on maximum achievable control technology, rather than based on health or risk.[11] The standards often do not eliminate emissions, and the remaining emissions may present or contribute to unreasonable risks. For this reason, there is no justification for EPA to exclude ambient air exposures to carbon tetrachloride from the risk evaluations, as proposed.[12] EPA's assertion that "any risks [are] effectively managed when under the jurisdiction of the CAA" has no legal or scientific basis since the CAA provisions governing hazardous air pollutants do not establish a risk-based program. At a minimum, there is no basis for concluding that "unreasonable risk" within the meaning of TSCA, including consideration of potentially exposed and susceptible subpopulations, are "effectively managed" through CAA regulation.[13] Similarly, EPA cannot simply assume that risks are adequately addressed by RCRA. As EPA is well aware, the agency's RCRA regulations are riddled with exclusions and exemptions that limit RCRA's reach, including the protections offered by the Subtitle C "cradle to grave" hazardous waste requirements. Where those protections do not apply, there is no basis for EPA's claim that RCRA will sufficiently guard against risks.

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[11] 42 U.S.C. § 7412(d)(2).

[12] US EPA, *Problem Formulation of the Risk Evaluation for Carbon Tetrachloride*, at 43.

[13] *Id.* at 48.

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Moreover, even if regulations adopted under another environmental statute reduced exposure to a chemical, that exposure pathway must still be evaluated under TSCA unless **no** exposures are ongoing as a result of the regulation. As one of EPA's risk assessment handbooks explains, individuals may be exposed to chemicals "through more than one pathway. … [T]o achieve effective risk assessment and risk management decisions, *all* media and routes of exposure should be assessed."[14]

The 1,4-dioxane problem formulation illustrates why EPA's approach is so concerning. EPA indicates that it will exclude exposure to 1,4-dioxane from drinking water because this chemical is "currently being evaluated" under the SDWA.[15] EPA's proposal glosses over the fact that millions of people are currently drinking water contaminated with 1,4-dioxane, and will continue to do so for the foreseeable future.[16] Moreover, there is no certainty that EPA will ever take any measure under the SDWA to reduce these exposures. Even if EPA were to take some regulatory action under the SDWA, there is no way to know the level of continued exposure nor is there any assurance that the regulatory action will ensure "that the chemical substance . . . no longer presents [unreasonable] risk,"[17] as EPA would be required to ensure if such risks were identified as a result of the TSCA risk evaluation. Similar flaws are rampant in other problem formulations.

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[14] US EPA, *National Center for Environmental Assessment, Exposure Factors Handbook: 2011 Edition* 1-18 (2011) (emphasis added).

[15] US EPA, *Problem Formulation of the Risk Evaluation for 1,4-Dioxane*, at 43.

[16] *See* Declaration of Patricia D. Koman, Ph.D., M.P.P., In Support of Petitioners' Opening Brief, sworn April 13, 2018, submitted herewith as Exhibit 2; Declaration of Detlef Knappe, Ph.D. In Support of Petitioners' Opening Brief, sworn April 11, 2018, submitted herewith as Exhibit 3. These declarations were submitted by Petitioners in *Safer Chemicals, Healthy Families v. US EPA*.

[17] 15 U.S.C. § 2605(a).

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EPA's approach is counter to section 9 of TSCA, which governs EPA's options when laws other than TSCA, but that are administered by EPA, could eliminate or sufficiently reduce risks posed by chemical substances. Under section 9(b), EPA can choose to "protect against [a] risk" that has *already been identified in a TSCA risk evaluation* by using its non-TSCA authorities to manage the identified risks.[18] However this provision applies only *after EPA has completed a risk evaluation* and found unreasonable risk. Once an unreasonable risk determination is made, EPA can decide to "protect against such risk" under a law other than TSCA if it first "determines that a risk to health or the environment associated with a chemical substance or mixture could be eliminated or reduced to a sufficient extent by actions taken under the authorities contained in such other Federal laws."[19] The fact that EPA can look to other environmental statutes to "protect against [a] risk" identified in a TSCA risk evaluation, does not give EPA license to ignore exposures that *might be* reduced, in the future under a different law, when it conducts the TSCA risk evaluation.

In sum, TSCA does not permit EPA to exclude "conditions of use" or exposure pathways from a risk evaluation conducted under section 6(b), as proposed in the problem formulations. If EPA does not change course, such that these and other similar exclusions of conditions of use and their resulting exposures are reflected in the risk evaluations, the resulting risk evaluations will violate TSCA's plain text, structure, and purpose.

B. The problem formulations violate TSCA by excluding so-called legacy uses and associated disposals

Several of the problem formulations propose to exclude exposures from so-called "legacy uses," "associated disposal," and "legacy disposal" -- in other words, exposures from the

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[18] *See id.* § 2608(b)(1).

[19] *Id.*

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ongoing use and disposal of chemicals that are no longer manufactured for the use that is deemed "legacy." EPA asserts that these uses and disposals are not "conditions of use" within the meaning of TSCA. But this approach overlooks that the definition of "condition of use" includes "the circumstances . . . , under which a chemical substance is intended, known, or reasonably foreseen to be . . . used, or disposed of," irrespective of whether it is also manufactured, processed, or distributed in commerce. Because the TSCA definition of "conditions of use" uses a disjunctive "or" list, each lifecycle stage of a chemical, standing alone, is a condition of use, even if some of the chemical's lifecycle stages have been discontinued. EPA's proposed construction in the problem formulations robs the words "use" and "disposal" of their clear, independent role in the statute. For the reasons set forth in Petitioners' Opening Brief at 40-51, EPA's "rewriting [of TSCA's] unambiguous statutory terms" cannot stand. *Util. Air Regulatory Grp. v. EPA*, 134 S. Ct. 2427, 2445 (2014).

Not only is EPA's approach illegal under TSCA, it will also leave the population at significant risk of harm from toxic exposures. For example, in the problem formulation for HBCD, EPA proposes to exclude exposures to HBCD related to its use as a flame retardant in high impact polystyrene (HIPS) in electronic components. This is based on EPA's assertion that HBCD is no longer used in HIPS. However, until recently, HBCD was used extensively as an additive flame retardant in casings for electronics such as TVs, DVD players, and computers that were made of HIPS, and as a result, many people *continue to be exposed to HBCD* from electronics in their homes. Indeed, a recent study found a significant correlation between the number of electronics in the home and the amount of HBCD on people's hands (an exposure metric used to estimate dermal absorption and hand-to-mouth ingestion), indicating that

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electronics are a significant source of exposure for people.[20] EPA's problem formulation acknowledges these ongoing exposures. In the Executive Summary of the HBCD problem formulation, EPA states: "In indoor environments, there may also be exposures resulting from legacy uses of HBCD in articles (textiles, electronics and electrical products) containing HBCD."[21] Yet, inexplicably, EPA is proposing to exclude these consumer exposures from ongoing uses of products containing HBCD from the risk evaluations. This result is especially wrong-headed given that there is a robust marketplace for "used electronics" in this country, as is evident on eBay, craigslist, and the like. In light of the known ongoing exposures to HBCD from HIPS in electronics, it is unconscionable and illegal for EPA to exclude this exposure pathway from its risk evaluation.

EPA should modify the problem formulations to bring them into line with congressional intent that all exposures from use and disposal be addressed in section 6(b) risk evaluations so that evaluation and management of chemicals truly protects against unreasonable risk.

C. The problem formulations ignore known exposed and susceptible subpopulations

Under TSCA section 6(b), each risk evaluation must consider "whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other nonrisk factors, *including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the*

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[20] Tay JH *et al.* Assessment of Dermal Exposure to Halogenated Flame Retardants: Comparison Using Direct Measurements from Hand Wipes with an Indirect Estimation from Settled Dust Concentrations. 115:285–94 (2018). Additional information about residential exposure to HBCD is set forth in the Declaration of Veena Singla, Ph.D. In Support of Petitioners' Opening Brief, sworn April 3, 2018, a copy of which is submitted herewith as Exhibit 4.

[21] US EPA, *Problem Formulation for Cyclic Aliphatic Bromides Cluster*, at 10.

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Administrator, under the conditions of use."[22] The statutory requirement to consider risks to potentially exposed or susceptible subpopulations runs throughout section 6(b). Despite this clear mandate, EPA's problem formulations propose to narrow the set of "susceptibilities" that would put certain subpopulations "at greater risk than the general population of adverse health effects from exposure,"[23] as compared to the Scope documents published in July 2017.

For 1-bromopropane, for example, in section 2.4.2.3 of the Scope, entitled "Potentially Exposed or Susceptible Subpopulations," EPA indicates that it considers pregnant women and infants to be vulnerable populations, referencing findings of developmental toxicity in a rodent study and indicating that the study is "representative of a sensitive subpopulation (i.e., adult women of childbearing age and their offspring)."[24] However, in the parallel section 2.4.2.3 of the Problem Formulation, EPA fails to reference a single vulnerable population. Rather, it states that "[i]n developing the hazard assessment, EPA will evaluate available data to ascertain whether some human receptor groups may have greater susceptibility than the general population to the chemical's hazard(s)."[25] In other words, without explanation, EPA no longer references adult women of childbearing age and their offspring as "sensitive subpopulations" when it comes to 1-bromopropane. This unexplained decision not to include adult women of childbearing age and their offspring as potentially exposed or susceptible subpopulation, despite being identified as such in the scope, is not permissible.

Similarly, for asbestos, EPA has removed age, pre-existing health conditions, genetic makeup/ genetic polymorphisms, co-exposure to other substances, early age at exposure,

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[22] 15 U.S.C. § 2605(b)(4)(A) (emphasis added).

[23] *Id.* § 2602(12).

[24] US EPA, *Scope of the Risk Evaluation for 1-Bromopropane,* 34 (2017).

[25] US EPA, *Problem Formulation of the Risk Evaluation for 1-Bromopropane*, at 45.

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smoking, and pre-existing respiratory conditions.[26] For TCE, it has removed life stage, gender-specific, genetic variation, race/ethnicity, preexisting health status, lifestyle factors and nutrition status from its list of factors that increase susceptibility to greater harm.[27] These inexplicable proposals to omit certain vulnerable populations from the risk evaluations are not permitted by TSCA. EPA must modify its approach to ensure that each of the problem formulations considers the greater exposures and greater susceptibilities of "potentially exposed and susceptible subpopulations," as the statute requires.

D. The problem formulations violate TSCA by excluding from their conceptual models conditions of use, exposure pathways, hazards, and potentially exposed and susceptible subpopulations that were included in the scope documents released in June 2017

Not only do the problem formulations describe an approach that would violate the *substantive* requirements of TSCA (insofar as they exclude known or reasonably foreseen hazards, exposure pathways, and conditions of use), moving forward with the new approach would violate the *procedures* mandated by TSCA. Specifically, TSCA section 6(b)(4)(D) precludes narrowing the hazards, exposures, conditions of use, and potentially exposed or susceptible subpopulations that were included in the scopes of the risk evaluations published in June 2017 (scopes). Under TSCA, after EPA initiates a risk evaluation, it must "publish *the scope of the risk evaluation to be conducted*, including the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations the Administrator expects to consider."[28] Nothing in TSCA authorizes EPA to issue a "problem formulation" document after

[26] US EPA, *Scope of the Risk Evaluation for Asbestos,* 35 (2017).

[27] US EPA, *Scope of the Risk Evaluation for Trichloroethylene,* 38 (2017).

[28] 15 U.S.C. § 2605(b)(4)(D) (emphasis added).

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the scoping process, and it certainly does not authorize EPA to use such a document to narrow the published scope of the risk evaluation.

EPA's approach is especially concerning because the parameters of "the scope of the risk evaluation" published pursuant to this section have legal consequences. For example, "the scope of the risk evaluation" determines the extent that EPA's actions preempt state actions involving the chemicals evaluated under TSCA section 6(b). Under TSCA section 18(b)(1), once EPA "defines the scope of a risk evaluation for a chemical substance under section 2605(b)(4)(D)," no State may establish a statute, criminal penalty, or administrative action prohibiting or restricting the manufacture, processing, distribution in commerce, or use of such chemical substance until EPA issues a risk evaluation or its time to do so expires. Under TSCA section 18(c)(2), federal preemption applies only to "the hazards, exposures, risks, and uses or conditions of use of such chemical substances included in the scope of the risk evaluation pursuant to section 2605(b)(4)(D) of this title."[29] If EPA establishes "the scope of the risk evaluation," but then narrows that scope — as it is proposing to do here — States would arguably be preempted from regulating hazards, exposures, and risks that EPA is not addressing in its risk evaluation, merely because these hazards, exposures and risks were (fleetingly) included in the Scope. This would undermine the right and ability of states to regulate to protect their citizens where EPA has chosen to stand to the side.

For this reason, EPA cannot now backtrack on the June 2017 scopes by excluding hazards, exposure pathways, susceptible populations and conditions of use that were included in the June 2017 scopes. Instead, EPA must analyze all of these factors and their contribution to the risk posed by the chemical substance.

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[29] *Id.* § 2617(c)(2).

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E. The problem formulations indicate that EPA is proposing to base the risk evaluations on unreliable or incomplete information in violation of TSCA

TSCA requires EPA to consider "information" relating to a chemical that is "reasonably available to the Administrator" throughout the risk evaluation process.[30] So that EPA can obtain and develop "the information necessary to fill knowledge gaps before making regulatory decisions,"[31] Congress expanded EPA's information-gathering authorities as part of the 2016 amendments to TSCA.[32]

1. Failure to rely on meaningful information

Despite the requirement that EPA rely on reasonably available information, the problem formulations suggest that EPA is relying on unfounded conjecture, incomplete, ambiguous, and self-serving reports by a subset of manufacturers and processors, or in some cases on the *absence* of information. This approach is incompatible with the TSCA requirements to base decisions on reasonably available information and the best available science.[33]

The HBCD problem formulation illustrates these concerns, which are present in the other problem formulations as well. EPA appears to be rejecting reliable evidence that HBCD continues to be used in consumer products, but with no justification. For example, EPA notes "[f]rom June 2012 to March 2017, the use of HBCD in children's clothing and blankets was self-reported 44 times by manufacturers and retailers to Washington State under state law."[34] Despite what appears to be clear evidence that HBCD is used in textiles, EPA inexplicably

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[30] *Id.* § 2625(k).

[31] H.R. Rep. No. 114-176, at 22 (2015).

[32] *See id.*; 15 U.S.C. §§ 2603(a)(1), (a)(2).

[33] *See id.* §§ 2625(h), (k).

[34] US EPA, *Problem Formulation for Cyclic Aliphatic Bromides Cluster,* at 22.

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proposes to exclude this use from the risk evaluation, stating that "[i]nformation gathered from research, industry and consumer product organizations has led EPA to believe that HBCD is no longer used in consumer textiles. Current use in consumer textiles has not been confirmed and EPA does not believe it is known, intended, or reasonably foreseen. Therefore, use in consumer textiles is not a condition of use under which EPA will evaluate HBCD."[35] Excluding uses based on conjecture that is inconsistent with clear evidence cannot be squared with the informational requirements and scientific standards in TSCA section 26.

In addition, EPA asserts that HBCD is no longer used in the production of flame retardants, EPS resins, high impact polystyrene, XPS masterbatch, motor vehicle upholstery, consumer textiles, and military, institutional and aviation textile applications. As a result, EPA plans to exclude these uses from the risk evaluation because it considers them not to be "conditions of use."[36] But these critical exclusions are based primarily on self-serving assertions from a subset of HBCD manufacturers, or the absence of information. For example:

- EPA states that "no information was identified that confirms use of HBCD in recycled HIPS for the purposes of flame retardancy. EPA, therefore, does not believe that this use is intended, known, or reasonably foreseen and is not a condition of use for HBCD." [37]
    - EPA cannot exclude uses based on the absence of information.
    - EPA cannot act based on "belief," rather than information.
    - It is irrelevant whether HBCD is present for purposes of flame retardancy.

- EPA states: "Albemarle Corporation, another historic manufacturer of HBCD, indicated that they stopped manufacturing HBCD flame retardants around 2016 and do not intend to resume the manufacture of HBCD-based flame retardants."[38]
    - What will ensure that Albemarle does not change its "intention" and resume manufacture? In the absence of a legal restriction on resumed manufacture, this intention should not be a basis of excluding uses from the risk evaluation.

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[35] *Id.*

[36] US EPA, *Problem Formulation for Cyclic Aliphatic Bromides Cluster*, at 24-25.

[37] *Id.* at 21.

[38] *Id.* at 20.

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- Even if Albemarle is true to its "intention," what will ensure that other manufacturers do not start the manufacture of HBCD-based or even HCBD containing flame retardants given the market "opening" by Albemarle's withdrawal?

- EPA states: "The EPS Industry Alliance (EPS-IA) which represents all major North American manufacturers (including Canada and Mexico) of EPS resin, reports that its members have phased out of the use of HBCD in the production of EPS resins."[39]
  - What assurance does EPA have that this "report" is accurate?
  - What about "non-major" manufacturers?

- EPA states that "Use of HBCD in High Impact Polystyrene (HIPs) appears to have ceased and EPA does not believe this use is intended, known, or reasonably foreseen."[40]
  - What does it mean that use "appears to have ceased"?
  - EPA cannot exclude uses based on belief, rather than information.

These are nothing more than speculative predictions about future events for which EPA has provided no evidence in support.

We also note that in the problem formulation for 1-bromopropane, EPA indicates that it will exclude many consumer uses of this substance, despite the fact that it is present in products that are generally available to consumers. EPA indicates that it will not consider consumer uses of 1-bromopropane as an adhesive because these products are "usually [sold] in amounts larger than consumers could use" and are sold through wholesale channels. EPA also indicates that it is excluding consumer use of 1-bromopropane as a brake cleaner and engine degreaser, despite the fact that many consumers do repair work on their own cars. EPA's theory is that 1-bromopropane has not been advertised for consumer use and expensive.[41] These evidence-less rationales for exclusion are not sufficient to conclude that consumers would not use this product.

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[39] *Id.* at 21.

[40] *Id.*

[41] US EPA, *Problem Formulation of the Risk Evaluation for 1-Bromopropane*, at 19.

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2. EPA cannot rely on uncertified chemical manufacturer's assertions that a product has been discontinued

Even if it were appropriate for EPA to exclude from its risk evaluations *truly discontinued* uses — and this would only be appropriate if there is no known, intended or reasonably foreseen ongoing use or disposal of the substance — EPA cannot conclude that a use is discontinued simply based on the agency's surmise that manufacture "appears" to have ceased, or that a manufacturer "indicated" that they are no longer making the substance. The fact that major manufacturers have ceased production does not mean that manufacture is not known or reasonably foreseeable, because it tells us nothing about minor manufacturers. Indeed, minor manufacturers can become major manufacturers once their larger competitors leave the business. Appearances, indications, beliefs, reports, and so on, do not constitute "information," and TSCA requires EPA to base its risk evaluations on "information."

For EPA to exclude a condition of use from its risk evaluation because use has discontinued, it must conduct an analysis based on all reasonably available information to confirm that re-commencement is not reasonably foreseen. And it must have in place a SNUR that prohibits the renewed manufacture and processing of all discontinued uses without notice to and review by EPA. Absent a meaningful analysis of whether resumption is reasonably foreseen, as well as SNURs that close the door on resumption, EPA would be excluding uses in the absence of reliable information.

3. EPA has failed to obtain all "reasonably available information" about asbestos and methylene chloride

The problem formulations for asbestos and methylene chloride indicate that EPA is not taking into account some of the most reliable information regarding the levels of workplace

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exposure to these substances. Under OSHA, every employer whose employees are at risk of exposure to asbestos must conduct periodic exposure monitoring, including monitoring of employees who are, or may reasonably be expected to be exposed to airborne concentrations" over levels set by OSHA.[42] The same is true for methylene chloride.[43] Records of this medical monitoring must be retained for 30 years.[44] EPA should ask all employers subject to these mandates to submit these records to EPA so the agency can rely on them in its risk evaluations. As there is "reasonably available" information regarding actual workplace exposures to asbestos and methylene chloride, EPA is obligated to consider it under TSCA section 26(k).[45]

F. EPA should not rely on the TSCA systematic review protocol in the risk evaluations

The TSCA systematic review protocol describes how EPA intends to identify, evaluate, and integrate scientific information used in TSCA risk evaluations. We urge EPA not to utilize the approach laid out in this document in developing the risk evaluations for the first ten chemicals. TSCA does not permit reliance on this approach because it is not consistent with best practices for systematic review (as detailed in comments submitted during this comment period from the University of California San Francisco Program on Reproductive Health and the Environment, and others). Rather than laying out a method for evaluating the quality of evidence, this protocol will result in the exclusion of studies that may contain valid scientific data. TSCA requires EPA to conduct risk evaluations "us[ing] scientific information, technical procedures, measures, methods, protocols, methodologies, or models, employed in a manner

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[42] 29 C.F.R. § 1910.1001(d)(2)(i).

[43] *Id.* § 1910.1052(d).

[44] *Id.* § 1910.1020(d)(1)(i).

[45] 15 U.S.C. § 2625(k).

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consistent with the best available science"[46] and reasonably available information.[47] The TSCA systematic review document lays out a protocol that is inconsistent with this mandate by excluding information from EPA's consideration based on a single reporting or methodological limitation even when the study provides some valid and meaningful information. TSCA section 26(h), (i) and (k) reveal Congress's intent that EPA gather all reasonably available information and give it the appropriate weight taking into account limitations. EPA's new TSCA systematic review protocol is antithetical to TSCA section 26 insofar as it will entirely exclude meaningful, scientifically valid information based on single-flaw thresholds. It would be legal error for EPA to continue to rely on this approach as it moves forward with its risk evaluations.

CONCLUSION

For the foregoing reasons, TSCA requires EPA to modify the problem formulations so its risk evaluations encompass all conditions of use, including for uses and disposal of substances no longer manufactured for these purposes, address risks to all potentially exposed and susceptible subpopulations, and are based on all reasonably available information and a systematic review protocol that is established through a transparent and scientific process that meets globally established best practices.

Submitted this 16th day of August 2018 by:

Earthjustice

Alaska Community Action on Toxics

Environmental Health Strategy Center

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[46] *Id.* § 2625(h).

[47] *Id.* § 2625(k).

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Environmental Working Group

Learning Disabilities Association of America

Sierra Club

Union of Concerned Scientists

United Steel, Paper and Forestry, Rubber, Manufacturing, Energy, Allied Industrial and Service Workers International Union, AFL-CIO/CLC

WE ACT for Environmental Justice

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Exhibit 1

IN THE UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

Docket No. 17-72260
Consolidated with Docket Nos. 17-72501, 17-72968, 17-73290, 17-73383, 17-73390

SAFER CHEMICALS, HEALTHY FAMILIES et al.,

Petitioners,

v.

U.S. ENVIRONMENTAL PROTECTION AGENCY et al.,

Respondents.

IPC INTERNATIONAL, INC. et al.,

Respondents-Intervenors.

On Petition for Review of Final Rules of the U.S. Environmental Protection Agency

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OPENING BRIEF OF PETITIONERS:

ALASKA COMMUNITY ACTION ON TOXICS; ALLIANCE OF NURSES FOR HEALTHY ENVIRONMENTS; ASBESTOS DISEASE AWARENESS ORGANIZATION; CAPE FEAR RIVER WATCH; ENVIRONMENTAL DEFENSE FUND; ENVIRONMENTAL HEALTH STRATEGY CENTER; ENVIRONMENTAL WORKING GROUP; LEARNING DISABILITIES ASSOCIATION OF AMERICA; NATURAL RESOURCES DEFENSE COUNCIL; SAFER CHEMICALS, HEALTHY FAMILIES; SIERRA CLUB; UNION OF CONCERNED SCIENTISTS; UNITED STEEL, PAPER AND FORESTRY, RUBBER, MANUFACTURING, ENERGY, ALLIED INDUSTRIAL AND SERVICE WORKERS INTERNATIONAL UNION, AFL-CIO/CLC; VERMONT PUBLIC INTEREST RESEARCH GROUP; and WE ACT FOR ENVIRONMENTAL JUSTICE

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CORPORATE DISCLOSURE STATEMENT

Pursuant to Federal Rule of Appellate Procedure 26.1, Petitioners Safer Chemicals, Healthy Families; Asbestos Disease Awareness Organization; Vermont Public Interest Research Group; Environmental Defense Fund; Alliance of Nurses for Healthy Environments; Cape Fear River Watch; Natural Resources Defense Council; Alaska Community Action on Toxics; Environmental Health Strategy Center; Environmental Working Group; Learning Disabilities Association of America; Sierra Club; Union of Concerned Scientists; WE ACT for Environmental Justice; and United Steel, Paper and Forestry, Rubber, Manufacturing, Energy, Allied Industrial and Service Workers International Union, AFL-CIO/CLC submit that they have no parent corporations and no publicly issued stock shares or securities. No publicly held corporation holds stock in any of the petitioners.

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PRELIMINARY STATEMENT

Toxic chemicals pervade our environment. Chemicals pollute our air, soil, and water, and contaminate our homes, workplaces, and consumer products.

Congress enacted the Toxic Substances Control Act (TSCA) in 1976 to give the U.S. Environmental Protection Agency (EPA or Agency) authority to "look comprehensively at the hazards associated with [a] chemical" and to prevent harm to health and the environment through regulation of chemicals posing unreasonable risks. S. Rep. No. 94-698, at 2 (1976). Nonetheless, the vast majority of chemicals in commerce have never been reviewed by EPA for safety and remain unregulated. This near-total failure to address chemical risks led Congress to amend TSCA in 2016, establishing a mandatory process to systematically evaluate and manage the risks of existing chemicals.

To implement this new mandate, Congress required EPA to issue two rules, known as the Framework Rules, establishing the processes by which EPA will prioritize chemicals for risk evaluations and then conduct those evaluations. The evaluation results—a finding of whether a chemical presents an unreasonable risk to health or the environment—dictate whether the Agency must ban, restrict, or otherwise regulate the chemical to prevent the risk.

Risk—the likelihood of harmful effects to human health or ecological systems—is determined by the toxicity of a chemical (i.e., its hazard) combined

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with how much contact (i.e., exposure) a person or ecological receptor has with the chemical.[1] Often, individuals are exposed to a chemical from multiple uses and through a variety of exposure pathways. Thus, TSCA can effectively protect against chemical harm only if EPA evaluates *all hazards and all exposures.* If EPA does not fully consider all known and reasonably foreseen hazards and exposures during a risk evaluation, the evaluation cannot accurately characterize the true risk posed by the chemical. Accordingly, the law requires EPA to examine broadly all of a chemical's "conditions of use," a term TSCA defines to encompass a chemical's entire lifecycle, starting with manufacture and processing, and continuing through distribution, use, and disposal.

EPA proposed the Framework Rules in January 2017 to implement Congress's mandate. The proposals complied with TSCA's requirement to comprehensively evaluate a chemical's hazards and exposures and make a holistic determination of whether the chemical presents an unreasonable risk of injury.

In the spring of 2017, a former chemical-industry advocate who had just been appointed by the new administration oversaw the final drafting of the Framework Rules. Following this appointment, EPA abruptly reversed course and adopted the approach favored by the chemical industry, in many instances revising

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[1] U.S. EPA, *About Risk Assessment*, https://www.epa.gov/risk/about-risk-assessment.

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the rules to match the chemical industry's comments word for word. In the final Framework Rules, EPA asserts unfettered discretion to exclude known or reasonably foreseen exposure pathways from consideration, thereby ignoring important contributors to a chemical's overall risk.

The Framework Rules unlawfully narrow the scope of risk evaluations by allowing EPA to exonerate chemicals based on only a partial review of known or reasonably foreseen uses and exposures. The Rules thereby threaten to leave the public—and especially vulnerable groups like children, pregnant women, and workers—inadequately protected from the potential risks of the thousands of chemicals to which individuals are exposed every day. Essential parts of the Rules violate Congress's unambiguous command to evaluate each chemical holistically and comprehensively, and those parts must be set aside.

STATEMENT OF JURISDICTION

Respondents EPA and Administrator Scott Pruitt (together, EPA) issued the Framework Rules pursuant to their authority under TSCA. 15 U.S.C. § 2605(b)(1)(A), (b)(4)(B); ER 1, 29.[2] The U.S. Courts of Appeals have jurisdiction to review the final Rules. 15 U.S.C. § 2618(a)(1)(B). Venue is proper in this Court because Petitioner Alaska Community Action on Toxics resides in

[2] Petitioners use "ER" to refer to the Excerpts of Record and "PA" to refer to Petitioners' Addendum of Declarations in Support of Standing.

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Alaska, and Petitioners Asbestos Disease Awareness Organization and Sierra Club reside in California. PA 5, 51, 321.

The Framework Rules were published on July 20, 2017, ER 1, 29, and issued for purposes of judicial review on August 3, 2017, *see* 40 C.F.R. § 23.5. Petitioners filed timely petitions for review in three Courts of Appeals on August 10 and 11, 2017. *See* 15 U.S.C. § 2618(a)(1)(A); Pet'rs' Joint Opp'n to Resps.' Mot. to Transfer 4-5, ECF No. 18 (listing petitions). All six petitions challenging the Rules were subsequently consolidated in this Court. Order, No. 17-1926 (4th Cir. Dec. 11, 2017), ECF No. 63; Order, No. 17-72260 (9th Cir. Jan. 3, 2018), ECF No. 34; *see* 28 U.S.C. § 2112(a)(3), (a)(5).

STATEMENT OF ISSUES PRESENTED

1. Congress directed EPA to conduct risk evaluations to determine whether "a chemical substance" presents an unreasonable risk of injury to health or the environment under "the conditions of use." 15 U.S.C. § 2605(b)(1)(A).

   a. Does TSCA grant EPA authority to pick and choose which conditions of use it will consider in prioritizing chemicals and conducting risk evaluations?

   b. Does TSCA permit EPA to conclude a risk evaluation without determining whether the chemical substance as a whole presents an unreasonable risk?

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c. Does TSCA permit EPA to determine that individual conditions of use do not present an unreasonable risk before completing its evaluation of the chemical substance as a whole?

2. Congress defined "conditions of use" as "the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of." 15 U.S.C. § 2602(4). Has EPA unlawfully rewritten this definition by excluding a chemical's ongoing and future use and disposal from "conditions of use" if the chemical's manufacture, processing, and distribution for that specific use have been discontinued?

3. Congress directed EPA to consider all "reasonably available" information when making priority designations and conducting risk evaluations. 15 U.S.C. § 2625(k). Are the Framework Rules contrary to this mandate or arbitrary and capricious because they (a) penalize incomplete submissions by public commenters; (b) create thresholds for considering scientific information; (c) allow manufacturers to withhold relevant information about a chemical when requesting risk evaluations; and/or (d) fail to require EPA to consider during prioritization whether it has adequate information to conduct a risk evaluation?

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STATUTORY ADDENDUM

Petitioners attach a separate Statutory Addendum to their Opening Brief. 9th Cir. R. 28-2.7.

STATEMENT OF THE CASE

I. The Toxic Substances Control Act

A. The unfulfilled promise of the 1976 enactment

Congress enacted TSCA in 1976 to "prevent unreasonable risks of injury to health or the environment" from chemicals. S. Rep. No. 94-698, at 1; Pub. L. No. 94-469, 90 Stat. 2003 (codified at 15 U.S.C. § 2601 et seq.) (1976). 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, at 7 (1976); *see* S. Rep. No. 94-698, at 3 ("[W]e have become literally surrounded by a man-made 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," S. Rep. No. 94-698, at 1, through a comprehensive approach to chemical risk management that considered "the full extent of human or environmental exposure," H.R. Rep. No.

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94-1341, at 6. However, the 1976 law proved ineffective at reducing risks to public health from toxic chemicals existing in commerce.

First, while TSCA section 6 required EPA to restrict unsafe chemicals, *see* 90 Stat. 2003, § 6(a), it did not establish a systematic process or schedule for evaluating whether chemicals present unreasonable risks of injury to health or the environment. As a result, EPA rarely restricted or banned existing chemicals, and these chemicals could remain in commerce indefinitely without any safety review by EPA. S. Rep. No. 114-67, at 4 (2015).

Second, EPA's use of section 6 was hampered by a court ruling invalidating EPA's 1989 ban on most uses of asbestos. *See Corrosion Proof Fittings v. EPA*, 947 F.2d 1201 (5th Cir. 1991). The court overturned EPA's asbestos rule on the grounds that EPA's cost-benefit analysis was flawed and that EPA failed to impose the "least burdensome" risk mitigation measure among available alternatives. *Id.* at 1215-17. Following this decision, EPA's section 6 rulemaking came to a standstill: EPA has not finalized a rule regulating an existing chemical under section 6 in nearly thirty years. S. Rep. No. 114-67, at 4. In fact, in the more than forty years since TSCA's enactment, EPA has only five times used its section 6 authority to ban, limit production of, or restrict the use of existing chemicals.[3]

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[3] *See* U.S. Gov't Accountability Office, *Chemical Regulation: Options Exist to Improve EPA's Ability to Assess Health Risks and Manage Its Chemical Review Program* 18 (June 2005), https://www.gao.gov/products/GAO-05-458.

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B. The 2016 amendments

In 2016, Congress overhauled TSCA by enacting the Frank R. Lautenberg Chemical Safety for the 21st Century Act (together with the 1976 law, the amended statute is referred to as TSCA). Pub. L. No. 114-182, 130 Stat. 448 (codified at 15 U.S.C. § 2601 et seq.) (2016). 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.

The 2016 amendments establish new requirements in section 6 for EPA to systematically evaluate the potential risks presented by existing chemicals. The Agency must now undertake a step-by-step process to (1) select, i.e., "prioritize" chemical substances needing evaluation based on their potential risk to health and the environment; (2) conduct "risk evaluations" of those prioritized chemicals, and some chemicals nominated by manufacturers, to determine whether they present unreasonable risks of injury to health or the environment; and (3) eliminate such risks by issuing rules regulating those chemicals. 15 U.S.C. § 2605(a)-(b).

Throughout the amendments to section 6, Congress used a new term, "conditions of use," to describe the circumstances EPA must consider when prioritizing chemicals for review and conducting risk evaluations. The statute broadly defines "conditions of use" as "the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or

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reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of." *Id.* § 2602(4). The amendments also clarified that EPA's "unreasonable risk" determination must be made "without consideration of costs" and removed the "least burdensome" requirement—modifying language that had doomed the asbestos ban. *Id.* § 2605(a), (b)(4)(A).

1. Prioritization

TSCA requires EPA to establish a "risk-based screening process," called prioritization, to guide EPA's selection of chemicals warranting full risk evaluation. Chemicals designated as "high-priority"—meaning they "may present an unreasonable risk of injury to health or the environment because of a potential hazard and a potential route of exposure under the conditions of use," *id.* § 2605(b)(1)(B)(i)—will undergo immediate risk evaluations. *Id.* § 2605(b)(3)(A). Chemicals designated as "low-priority"—a designation that must be based on "information sufficient to establish" that the chemical "does not meet the standard" for high-priority designation, *id.* § 2605(b)(1)(B)(ii)—will not undergo further review at that time. *Id.* § 2605(b)(1)(A).

2. Risk evaluations

Once EPA designates a chemical as high-priority, it must initiate a risk evaluation for that chemical and complete it within three years (with a possible six-month extension). *Id.* § 2605(b)(3)(A), (b)(4)(G). EPA must also conduct risk

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evaluations on some chemicals nominated by their manufacturer(s). *Id.* § 2605(b)(4)(C)(ii). Manufacturer-requested risk evaluations must follow the same process and meet the same requirements as EPA-initiated evaluations. *See id.* § 2605(b)(4)(C), (b)(4)(E)(ii).

Through each risk evaluation, EPA must

> determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other nonrisk factors … under the conditions of use.

Id. § 2605(b)(4)(A). EPA must evaluate risks not only to the general population, but also to relevant "potentially exposed or susceptible subpopulation[s]." *Id.* These include groups such as "infants, children, pregnant women, workers, or the elderly," that, "due to either greater susceptibility or greater exposure," may face greater risks of harm than the general population from chemical exposures. *Id.* § 2602(12).

As an initial part of the evaluation, EPA must publish the "scope" of the evaluation, describing "the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations the Administrator expects to consider." *Id.* § 2605(b)(4)(D). EPA must also, among other requirements, "integrate and assess available information on hazards and exposures for the conditions of use of the chemical substance." *Id.* § 2605(b)(4)(F)(i). This is because characterizing exposure involves gathering information on the various

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conditions of use of a chemical to determine the potential pathways of exposure to the chemical and estimate the extent of exposure to people or environmental receptors, including the duration, intensity, frequency, and number of exposures. *Id.* § 2605(b)(4)(F)(iv); *see* ER 52-54. Characterizing hazard involves reviewing scientific studies to determine the nature and severity of the harms caused by the chemical. ER 54-56. Ultimately, the risk evaluation will combine EPA's exposure and hazard assessments to estimate the risk the chemical presents. ER 56-57.

3. Risk management rules

If EPA determines "that the manufacture, processing, distribution in commerce, use, or disposal of a chemical substance or mixture, or that any combination of such activities, presents an unreasonable risk" to health or the environment, EPA must issue a rule under section 6(a) to address the risk. 15 U.S.C. § 2605(a), (c)(1). This rule must impose restrictions or other requirements designed to eliminate the unreasonable risk. *Id.* § 2605(a). Such requirements may include full or partial bans on manufacture, processing, or distribution; warning labels; recordkeeping requirements; use restrictions; and prohibitions or limits on methods of disposal. *Id.*

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4. Obtaining information

TSCA requires EPA to consider information relating to a chemical that is "reasonably available to the Administrator" throughout the prioritization and risk evaluation processes. *Id.* § 2625(k). To allow EPA to obtain and develop "the information necessary to fill knowledge gaps before making regulatory decisions," H.R. Rep. No. 114-176, at 23 (2015), Congress expanded EPA's information-gathering authorities as part of the 2016 amendments. *See id.* at 22-23; 15 U.S.C. § 2603(a)(1), (a)(2).

II. History of the Framework Rules

Congress required EPA to issue the Framework Rules to implement the amendments to section 6. 15 U.S.C. § 2605(b)(1)(A), (b)(4)(B).

A. The proposed Rules

EPA issued the proposed Prioritization and Risk Evaluation Rules on January 17 and 19, 2017, respectively. ER 577, 60.

The proposed Rules complied with TSCA's mandate to take a comprehensive approach to chemical risk evaluation. EPA explained in the proposed Prioritization Rule that, "in response to clear statutory directives," it would "designate the priority of a 'chemical substance,' as a whole," rather than "a specific use or subset of uses of a chemical substance." ER 581. In the proposed Risk Evaluation Rule, EPA likewise construed TSCA to require it to conduct risk

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evaluations on "the chemical substance," "not [on] individual conditions of use." ER 63. EPA's focus on the total risk posed by each chemical informed critical aspects of the proposed Rules.

First, the proposed Rules required EPA to consider during both prioritization and risk evaluation "*all* known, intended, and reasonably foreseen activities associated with the subject chemical substance," i.e., "*all* … activities that constitute the conditions of use within the meaning of [the statutory definition]." *Id.* (emphases added); *see* ER 582, 588. EPA applied the requirement to evaluate all of a chemical's conditions of use to both EPA-initiated and manufacturer-requested risk evaluations. ER 60, 75-76. As a result, the proposed Risk Evaluation Rule required manufacturers requesting risk evaluations to provide EPA with "all [reasonably available] information that is necessary for EPA to conduct a risk evaluation addressing all the circumstances that constitute [the chemical's] conditions of use." ER 74.

Second, the proposed Risk Evaluation Rule required EPA to make a single, final risk determination of whether "the chemical substance presents an unreasonable risk of injury." ER 78, 63.

B. Influence of Dr. Nancy Beck over the final Framework Rules

Until at least April 12, 2017, EPA continued to interpret TSCA as requiring risk evaluations to "encompass all" of a chemical's conditions of use, and relied on

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that interpretation in denying several citizen petitions under TSCA. *See* 82 Fed. Reg. 17,601, 17,603 (Apr. 12, 2017).

Shortly thereafter, however, the Trump Administration appointed Dr. Nancy Beck as Deputy Assistant Administrator for EPA's Office of Chemical Safety and Pollution Prevention, which oversees the TSCA program. Since joining EPA in late April 2017, Dr. Beck has been the senior political appointee under the Administrator responsible for all aspects of EPA's implementation of TSCA. For the five years immediately before joining EPA, Dr. Beck was the Senior Director for Regulatory Science Policy at Respondent-Intervenor American Chemistry Council (ACC). MA 63.[4] A registered lobbying organization, ACC is the principal advocacy association representing the nation's largest and most influential chemical manufacturers. *See* MA 53, 67-68; ER 82.

As one of ACC's chief advocates regarding EPA's implementation of TSCA, Dr. Beck presented ACC's recommendations for the Framework Rules at an EPA public meeting on August 9, 2016, and signed ACC's August 2016 comments elaborating on its desired approach for the Rules. ER 79, 82. ACC and Dr. Beck urged EPA to focus on subsets of chemicals' conditions of use in its risk

[4] Petitioners use "MA" to refer to the Motion Appendix (ECF No. 43-2) filed with their Motion to Complete the Administrative Records. The Motion requests that the Court compel EPA to complete the administrative records with the documents identified in paragraphs 3 through 20 of the Marks Declaration, as well as additional documents that EPA omitted from its certified records.

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evaluations. ER 86; *see also* MA 13, 17-18 (showing Dr. Beck's participation in a November 2016 meeting at the Office of Management and Budget at which ACC recommended that EPA not evaluate all conditions of use and instead focus on those uses "that present the highest likelihood of potential concern"). ACC's March 2017 comments on the Framework Rules, written while Dr. Beck remained at ACC, repeated the same positions as Dr. Beck's previous comments, including that EPA need not "include 'all' conditions of use in any particular risk evaluation." ER 137; *see* ER 606-07. Because of this prior advocacy on ACC's behalf, EPA's ethics office "advised" Dr. Beck that she "cannot participate in any meetings, discussions, or decisions that relate to any individual ACC comment nor attend any meeting at which ACC is present." MA 88.

Nonetheless, after Dr. Beck's arrival at EPA, the Agency abruptly reversed its interpretation of TSCA's requirements. The final Framework Rules upend EPA's prior approach to risk evaluations and significantly narrow the Agency's interpretation of the meaning of "the conditions of use." This altered approach ignored recommendations and concerns raised by career agency staff. *See* MA 25-27, 29-30. Many of the changes to the proposed Rules mirror ACC's specific requests, in many instances word for word. *See* MA 528-539.

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C. The final Rules

The Framework Rules reject the comprehensive, substance-based approach of the proposed Rules.

First, EPA now asserts in the Risk Evaluation Rule that TSCA grants EPA "discretion" to exclude conditions of use from its risk evaluation of a chemical. ER 4. The Rule establishes no criteria for such exclusions. This pick-and-choose interpretation extends to the Rule's provisions allowing manufacturers to request risk evaluations limited to the conditions of use they wish to include. 40 C.F.R. § 702.37(b)(3); *see* ER 12.

Second, the Risk Evaluation Rule allows EPA to conduct piecemeal risk evaluations for a chemical, without determining whether the "chemical substance" poses an unreasonable risk. Instead, the Rule directs EPA to determine whether individual conditions of use in isolation pose unreasonable risks. 40 C.F.R. §§ 702.47 (EPA "will determine whether the chemical substance presents an unreasonable risk … *under each condition of uses* [sic] within the scope of the risk evaluation" (emphasis added)), 702.49(d); *see* ER 19.

Third, the Framework Rules rewrite the statutory definition of "conditions of use" to omit consideration of a chemical's ongoing and future uses and related disposals if manufacturing, processing, and distribution for those specific uses are no longer occurring. ER 4-5, 31. EPA misleadingly labels these omitted activities

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"legacy uses," "associated disposal," and "legacy disposal." ER 4-5.

The Rules also limit EPA's ability to collect and consider reasonably available information necessary to inform its decisions under TSCA.

III. Risk evaluation actions to date

In December 2016, EPA selected the first ten chemicals to undergo risk evaluations under the amended TSCA and began those evaluations. 81 Fed. Reg. 91,927 (Dec. 19, 2016); *see* 15 U.S.C. § 2605(b)(2)(A). EPA released the scopes for these ten chemicals contemporaneously with the final Framework Rules. MA 520-22. The scopes rely on EPA's revised interpretations of TSCA incorporated into the Framework Rules. *See* 82 Fed. Reg. 31,592, 31,593 (July 7, 2017).

STANDARD OF REVIEW

The standard set forth in the Administrative Procedure Act applies to the Court's review of EPA rules implementing TSCA. 15 U.S.C. § 2618(c)(1). Under this standard, courts must "hold unlawful and set aside" agency action and conclusions "found to be … arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2).

When reviewing whether an agency's interpretation of a statute is lawful, the Court follows the test established in *Chevron U.S.A. Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837 (1984). *City of L.A. v. U.S. Dep't of Commerce*, 307 F.3d 859, 868 (9th Cir. 2002). If Congress has spoken directly to

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the precise question at issue, the Court must give effect to Congress's unambiguously expressed intent. *Chevron*, 467 U.S. at 843 & n.9; *Akhtar v. Burzynski*, 384 F.3d 1193, 1198 (9th Cir. 2004). If the statute is silent or ambiguous, a court will defer to an agency's reasonable interpretation. *Chevron*, 467 U.S. at 843 & n.9.

In addition, agency action is arbitrary and capricious where an agency "entirely fail[s] to consider an important aspect of the problem" or fails to articulate a "'rational connection between the facts found and the choice made.'" *Motor Vehicle Mfrs. Ass'n of U.S. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983) (quoting *Burlington Truck Lines v. United States*, 371 U.S. 156, 168 (1962)). A court's review of agency action, while "deferential," must be "thorough, probing, [and] in-depth." *Ranchers Cattleman Action Legal Fund United Stockgrowers of Am. v. U.S. Dep't of Agric.*, 415 F.3d 1078, 1093 (9th Cir. 2005) (internal quotation marks omitted).

SUMMARY OF ARGUMENT

1. EPA's claim of authority to exclude conditions of use and their resulting exposures from risk evaluations violates TSCA's plain text, structure, and purpose. The directive to "determine whether *a chemical substance* presents an unreasonable risk" requires an evaluation of the chemical's total risk. And the phrase "under *the* conditions of use" unambiguously means *all* of the chemical's

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conditions of use. Several provisions of TSCA confirm Congress's intent. First, when Congress intended EPA to act on fewer than all conditions of use, it expressly provided for such action. Second, Congress created a narrow exception allowing EPA to regulate certain chemicals based on previously completed risk assessments limited to a subset of conditions of use; this exception confirms that the new law otherwise requires comprehensive risk evaluations. Third, TSCA specifies in detail how EPA is to prioritize chemicals and evaluate their risks, but does not provide EPA with any criteria to eliminate conditions of use. Moreover, excluding conditions of use will frustrate TSCA's purpose of preventing unreasonable risks to health by underestimating risk, especially to vulnerable subpopulations. EPA's interpretation fails under *Chevron* and reflects arbitrary and capricious reasoning.

2. EPA also asserts authority to find that individual conditions of use, standing alone, do not present an unreasonable risk, and that it need not make a risk determination for a chemical substance as a whole. EPA's use-by-use approach cannot be reconciled with TSCA's requirement that EPA make a single, holistic risk determination on "a chemical substance."

3. EPA unlawfully rewrites the definition of "conditions of use" to omit a chemical's current and future use and disposal if the chemical's manufacture, processing, and distribution for that specific use are not ongoing. Congress's

inclusion of "use" and "disposal" as "conditions of use" forecloses this construction. 15 U.S.C. § 2602(4). Moreover, Congress consciously allowed EPA to prioritize and evaluate chemicals that have not been manufactured in the ten years prior to passage of the TSCA amendments, i.e., chemicals that have *only* conditions of use ("use" and "disposal") that EPA claims it may omit from analysis. EPA's rewrite thus finds no support in the text or structure of TSCA.

4. The Framework Rules are inconsistent with EPA's duty to "take into consideration" all "reasonably available" information when prioritizing chemicals and conducting risk evaluations. 15 U.S.C. § 2625(k). For example, the Risk Evaluation Rule penalizes any "incomplete" public submissions, chilling public participation. The Rule also impermissibly limits the information manufacturers must provide when requesting a risk evaluation, allowing them to withhold relevant information about a chemical. These information-limiting provisions inhibit the scientifically sound decisions EPA is required to make under section 6.

5. Petitioners have standing to challenge the Framework Rules because their members face a credible threat of injury from EPA's unlawful approach to prioritizing chemicals and evaluating their risks. Petitioners also have informational standing to challenge the Risk Evaluation Rule, and some Petitioners have organizational standing to challenge that Rule.

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ARGUMENT

I. The Framework Rules violate TSCA's mandate that risk evaluations consider all of a chemical's conditions of use

Under TSCA, EPA must conduct risk evaluations to determine whether "*a chemical substance* presents an unreasonable risk … under *the conditions of use*." 15 U.S.C. § 2605(b)(4)(A) (emphases added). This directive expresses Congress's clear intent that EPA evaluate the risks posed by "a chemical substance" as a whole, taking into account all circumstances comprising "the conditions of use" of the chemical.

Ignoring Congress's unambiguous direction, the Framework Rules grant EPA unfettered "discretion" to pick and choose which conditions of use it will include in each risk evaluation. ER 4-5. In other words, EPA claims authority to "exclude certain activities that EPA has determined to be conditions of use" from risk evaluations. ER 4.[5] The Risk Evaluation Rule codifies this pick-and-choose approach by providing that the scope of each evaluation will "include" only "[t]he

[5] To the extent the Prioritization Rule authorizes EPA to exclude conditions of use from consideration when designating a chemical as high- or low-priority, the Rule is likewise unlawful. *See* ER 31 (referring to EPA's "discretion to 'determine' the conditions of use" for each chemical); *compare* 40 C.F.R. § 702.9(f) (basing proposed low-priority designations on "the proposed conclusion that the chemical substance meets the definition of Low-Priority Substance … *under the activities that [EPA] determines constitute conditions of use*" (emphasis added)), *with* ER 588 (basing low-priority designations on consideration of "all uses that [EPA] determines constitute conditions of use").

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condition(s) of use, as determined by the Administrator, *that the EPA plans to consider*," giving EPA carte blanche to exclude any conditions of use it chooses. 40 C.F.R. § 702.41(c)(1) (emphasis added). The Rule repeatedly refers to "the conditions of use *within* the scope of the evaluation," indicating that some conditions of use are outside the evaluation's scope. 40 C.F.R. §§ 702.41(a)(5), (a)(8), (a)(9), (c)(4)(i), (c)(4)(iii), (d)(2); 702.49(b), (c), (d) (emphasis added). Similarly, the Rule allows EPA to limit an evaluation requested by a manufacturer to those conditions of use "identified in the request," and other limited conditions of use that "warrant inclusion." *Id.* § 702.37(e)(3); *see id.* § 702.37(b)(3).

EPA points to a smorgasbord of potential exposure pathways it may exclude, while also leaving open the possibility of other exclusions as well. *See* ER 5 (asserting it may exclude a chemical's presence as an "impurity"), 183-85 (suggesting it may exclude use as an intermediate chemical during manufacturing, the incidental manufacturing of a chemical as a byproduct, and uses "where other agencies hold jurisdiction").

EPA's interpretation is not only contrary to the "particular statutory language at issue" and "the language and the design of the statute as a whole," *McCarthy v. Bronson*, 500 U.S. 136, 139 (1991) (quoting *K Mart Corp. v. Cartier, Inc.*, 486 U.S. 281, 291 (1988)), but also frustrates TSCA's purposes by ignoring exposures and underestimating risks posed by chemicals, *see Wilderness Soc'y v.*

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U.S. Fish & Wildlife Servs., 353 F.3d 1051, 1060 (9th Cir. 2003) (en banc). If EPA excludes conditions of use during prioritization and risk evaluations, it cannot fulfill TSCA's command to determine whether "a chemical substance" poses an unreasonable risk to health or the environment. 15 U.S.C. § 2605(b)(4)(A). The Court must give effect to Congress's "unambiguously expressed intent" by setting aside the provisions of the Framework Rules that reflect EPA's illegal approach. *Chevron*, 467 U.S. at 843.

A. TSCA's plain language requires EPA to include all conditions of use in prioritization and risk evaluations

The starting point for construing TSCA "is the language of the statute itself." *Grp. Life & Health Ins. Co. v. Royal Drug Co.*, 440 U.S. 205, 210 (1979).

1. TSCA requires priority designations and risk evaluations to focus on "a chemical substance" as a whole

Congress consistently used the phrase "a chemical substance" to describe the object of priority designations and risk evaluations. 15 U.S.C. § 2605(b)(1)-(4), (i) (using the phrase fourteen times). This language requires EPA to consider all hazards and exposures that contribute to the total risk presented by the chemical substance as a whole.

This whole-substance focus begins during prioritization. The definitions of high- and low-priority substances make clear that it is the "substance" that receives the designation, not selected uses. *See id.* § 2605(b)(1)(B). As EPA recognized in

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the Prioritization Rule, "[t]he statute is clear that EPA is to designate the priority of the 'chemical substance'—not a condition of use for a chemical substance." ER 31 (citing 15 U.S.C. § 2605(b)(1)(A)).

EPA must also conduct risk evaluations on "a chemical substance" as a whole. For example, TSCA provides that "[u]pon designating a chemical substance as a high-priority substance, the Administrator shall initiate a risk evaluation on *the substance*." 15 U.S.C. § 2605(b)(3)(A) (emphasis added). Similarly, the statute directs EPA to determine either that "*a chemical substance* presents" or "does not present an unreasonable risk." *Id.* § 2605(i)(1)-(2) (emphasis added). Congress also uses the phrase "a chemical substance" or "chemical substances" in many other places in TSCA's risk evaluation provisions. *See, e.g.*, *id.* § 2605(b)(4)(G) (setting deadlines for completing evaluation for "a chemical substance"), (b)(2)(A), (b)(2)(B), (b)(3)(A), (c)(1).

Together, these provisions show that "the statute requires" EPA to determine "whether a chemical substance, as a whole, presents an unreasonable risk or [sic] injury." ER 63-64. As EPA previously concluded, an interpretation allowing the Agency to evaluate "merely a subset of individual uses" is "a strained reading" of section 6(b). *Id.*

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2. The phrase "the conditions of use" means *all* conditions of use

By requiring EPA to determine whether a chemical substance presents an unreasonable risk "under *the* conditions of use," 15 U.S.C. § 2605(b)(4)(A) (emphasis added), TSCA is unambiguous: EPA's evaluation must include *all* conditions of use of the chemical. The "definite article 'the' particularizes the subject which it precedes," in contrast to the "indefinite or generalizing force of 'a.'" *In re Cardelucci*, 285 F.3d 1231, 1234 (9th Cir. 2002) (quoting Black's Law Dictionary 1477 (6th ed. 1990)). When "the" precedes a collective or plural noun, it is equivalent to "all." *E.g.*, *Dutcher v. Matheson*, 840 F.3d 1183, 1194 (10th Cir. 2016); *Kaufman v. Allstate N.J. Ins. Co.*, 561 F.3d 144, 155 (3d Cir. 2009); *Frazier v. Pioneer Americas LLC*, 455 F.3d 542, 546 (5th Cir. 2006). Accordingly, the phrase "the conditions of use" means *all* conditions of use.

When Congress intended EPA to act on fewer than all of a chemical's conditions of use, it used different words to convey that intent. *See SEC v. McCarthy*, 322 F.3d 650, 656 (9th Cir. 2003). Congress allowed EPA to grant exemptions from risk management rules for "a specific condition of use" of a chemical, 15 U.S.C. § 2605(g)(1); directed EPA to consider reasonably available alternatives when deciding whether to ban or restrict "a specific condition of use," *id.* § 2605(c)(2)(C); and permitted EPA to allow test marketing for "specific conditions of use" of new chemicals in some circumstances, *id.* § 2604(h); *see also*

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id. § 2613(b)(4)(B)(i) (referring to "a specific condition of use"). The Court "must assume that this difference in language is legally significant." *Spencer Enters., Inc. v. United States*, 345 F.3d 683, 689 (9th Cir. 2003).

B. EPA's conclusion that it may exclude conditions of use is contrary to TSCA's structure

Because courts "construe statutes, not isolated provisions," *King v. Burwell*, 135 S. Ct. 2480, 2489 (2015) (internal quotation marks omitted), "the words of a statute must be read in their context and with a view to their place in the overall statutory scheme," *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 133 (2000) (internal quotation marks omitted).

1. EPA's pick-and-choose approach cannot be squared with the overall structure of TSCA

As EPA concluded in its proposed Risk Evaluation Rule, that TSCA "provides no criteria for EPA to apply" shows that the Agency does not have "license to choose among conditions of use." ER 64. The precision with which Congress prescribed EPA's implementation of section 6 supports this reading. Section 6 lays out detailed directions for EPA. *See* 15 U.S.C. § 2605(b)(1)(A) (mandating considerations for priority designations), (b)(4)(D) (identifying risk factors to include in a risk evaluation's scope), (b)(4)(F)(i)-(v) (detailing requirements for conducting risk evaluations); *see also id.* § 2605(a) (specifying possible risk management measures). These provisions indicate that Congress did

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not mean to allow EPA to exclude conditions of use from prioritization or risk evaluation without any criteria or instruction. *Cf. NRDC, Inc. v. EPA*, 863 F.2d 1420, 1432 (9th Cir. 1988) (invalidating regulatory procedure that "is wholly silent as to what factors the agency is to consider in granting exceptions" and provides "no discernible standard [for] limit[ing] th[at] discretion").

Indeed, when Congress intended EPA to exercise discretion under TSCA, it said so explicitly. *See, e.g.*, 15 U.S.C. §§ 2613(f) (granting EPA "[d]iscretion" in handling claims to protect confidential information), 2608(a) (instructing EPA, if it "determines, in the Administrator's discretion," that an unreasonable risk may be prevented under a federal law administered by another agency, to notify the agency), 2608(b), 2605(b)(4)(E)(iv)(II). That Congress purposefully included the language of discretion "in one section of the statute but omit[ted] it in another section of the same Act" shows that Congress did not intend EPA to use discretion to pick and choose which conditions of use to consider in prioritization and risk evaluation. *Hernandez v. Ashcroft*, 345 F.3d 824, 834 (9th Cir. 2003) (quoting *Andreiu v. Ashcroft*, 253 F.3d 477, 480 (9th Cir. 2001) (en banc)).

Underscoring that the pick-and-choose approach is inconsistent with TSCA's structure is EPA's suggestion that it may exclude "[u]ses where other agencies hold jurisdiction." ER 5. Congress is plainly aware, for example, that the Occupational Safety and Health Administration (OSHA) also has jurisdiction over

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worker safety, but section 6(b), when read with the definition of "potentially exposed or susceptible subpopulation," specifically requires EPA to evaluate the risks to workers. 15 U.S.C. §§ 2602(12), 2605(b)(4)(A). Further, section 9(c) permits concurrent EPA and OSHA regulation over working conditions. *See id.* § 2608(c). And, section 9 expressly contemplates that EPA may—only after it determines that a chemical presents an unreasonable risk—determine that the risk "may be prevented or reduced to a sufficient extent by action taken under a Federal law not administered" by EPA. *Id.* § 2608(a). These provisions show that Congress intended EPA to evaluate all conditions of use, even those potentially under the jurisdiction of other agencies. Indeed, where Congress intended to exclude uses of a chemical because they fall under the jurisdiction of another agency, it did so expressly. *See id.* § 2602(2)(B) (excluding from the definition of "chemical substance" uses regulated by other agencies under statutes such as the Food, Drug, and Cosmetic Act).

Similarly, EPA suggests that it may exclude conditions of use for reasons that bear no relationship to risk. *See* ER 5, 183-85. Such exclusions violate TSCA's requirement that EPA evaluate a chemical's risk "without consideration of costs or other nonrisk factors." 15 U.S.C. § 2605(b)(4)(A).

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2. TSCA's exception allowing certain partial risk evaluations confirms that comprehensive risk evaluations are the general rule

The express, limited exception Congress created to allow EPA to act on partial risk evaluations conducted prior to the 2016 TSCA amendments further confirms that Congress otherwise intended EPA to consider all conditions of use in risk evaluations. *See* 15 U.S.C. § 2625(*l*)(4). Section 26(*l*)(4) authorizes EPA to issue risk management rules for chemicals that, prior to the 2016 amendments, had been subject to partial risk evaluations based on a subset of conditions of use.[6] *Id.* Congress enacted this provision in direct response to concerns raised by EPA during the legislative process that partial risk evaluations were "simply not contemplated under the House and Senate bills." *See* MA 541. EPA noted that, absent this carve-out, the pending legislation would require EPA "to assess a chemical in its entirety, based on *all* conditions of use," and would preclude EPA from acting on its 2014 partial risk evaluations. *See* MA 540-42. Construing TSCA to allow EPA to conduct partial risk evaluations outside of this narrow carve-out, as the Framework Rules do, impermissibly renders section 26(*l*)(4) meaningless. *See Bilski v. Kappos*, 561 U.S. 593, 607-08 (2010). Although EPA now espouses a new view of this statutory language, its statement "to Congress …

[6] *E.g.*, trichloroethylene, 82 Fed. Reg. 7432, 7433 (proposed Jan. 19, 2017); methylene chloride and n-methylpyrrolidone, 82 Fed. Reg. 7464, 7465 (proposed Jan. 19, 2017).

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at the very time it presented its own amendment to the Congress as one it urged for adoption … [is] more reliable." *United States v. One Bell Jet Ranger II Helicopter*, 943 F.2d 1121, 1126 (9th Cir. 1991).

C. Excluding conditions of use will frustrate TSCA's aim to prevent unreasonable risks to health from toxic chemicals

The meaning of statutory language "depends on context," including the statute's objectives. *Brower v. Evans*, 257 F.3d 1058, 1065 (9th Cir. 2001) (internal quotation marks omitted); *see Crandon v. United States*, 494 U.S. 152, 158 (1990). TSCA's overriding purpose is to eliminate "unreasonable risk[s] of injury to health or the environment" associated with chemicals, *see* 15 U.S.C. §§ 2601(b), 2605(a), by authorizing EPA to "look comprehensively at the hazards associated with the chemical," S. Rep. No. 94-698, at 2; *supra* p. 6. Congress amended TSCA to promote "effective implementation" of the 1976 law's objectives. *See* S. Rep. No. 114-67, at 2. Thus, the TSCA amendments reaffirm EPA's obligation to comprehensively evaluate the risks of chemicals, for example by defining "conditions of use" broadly to encompass a chemical's whole lifecycle and mandating that EPA protect vulnerable subpopulations. *See* 15 U.S.C. §§ 2602(4), 2605(b)(4)(A).

Preventing unreasonable risk from a chemical requires EPA to consider all sources and pathways of exposure. As one of EPA's risk assessment handbooks explains, individuals may be exposed to chemicals "through more than one

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pathway. … [T]o achieve effective risk assessment and risk management decisions, *all* media and routes of exposure should be assessed." ER 248 (emphasis added). As public commenters explained, "a worker may be exposed to a chemical both at home and in the workplace, while an infant may be exposed to a chemical both through breast milk and through household dust." ER 253; *see also* ER 260. Additionally, an individual's exposure to a chemical through a single pathway (e.g., drinking water) may result from multiple uses of the chemical. *See* MA 29-30; ER 269, 272. "Even small exposures can add up over time to cause serious harm." ER 249. As EPA explained in the proposed Risk Evaluation Rule, if the Agency "were free to base its determination of whether a chemical substance, as a whole, presents an unreasonable risk … on merely a subset of individual uses, it could, for example, determine that a chemical substance with 10 known uses does not present an unreasonable risk of injury" after evaluating "a single one of those uses," while neglecting to evaluate other uses that may contribute to the chemical's risks. ER 63-64. This principle also explains why EPA must designate a chemical as high-priority if it lacks sufficient information to determine whether the chemical may present an unreasonable risk (including an unreasonable risk to vulnerable subpopulations). 15 U.S.C. § 2605(b)(2)(B). EPA cannot rule out the possibility that a chemical presents an unreasonable risk unless it has sufficient information on all conditions of use, because each condition of use

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may contribute to the chemical's total risk.

For the same reasons, excluding uses undermines the TSCA amendments' express commitment to protecting "potentially exposed or susceptible subpopulations," such as children, the elderly, and workers, from unreasonable chemical risks. *See* 15 U.S.C. § 2605(b)(1)(B)(i), (b)(4)(A), (b)(4)(F)(i). These subpopulations are defined by their "greater susceptibility or greater exposure" to chemicals, which may lead them to be "at greater risk than the general population of adverse health effects from exposure to a chemical." *Id.* § 2602(12). They face greater harm from low-level exposures, and may have more frequent exposures, from more sources, over time than the general population. *See, e.g.*, ER 275, 278 (children have "unique vulnerabilities to toxic chemicals," especially from "chronic, low-dose exposures that may occur at [developmentally] significant times"), 280-81, 284-87 (communities reliant on subsistence fishing and "wild foods" may face greater exposure to pollutants), 289, 290-91 (bio-accumulation of toxic chemicals in fish may increase exposure to individuals reliant on a "traditional subsistence diet"); *see also* ER 262-63, 298. To assess exposures to these vulnerable subpopulations in "real-world situations," EPA must consider "the totality of exposures from multiple pathways." ER 323 (citing U.S. EPA, Guidelines for Human Exposure Assessment, Risk Assessment Forum, Peer Review Draft (2016)).

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In sum, TSCA's text, structure, and purpose show that Congress spoke clearly to require EPA to include all conditions of use in making a priority designation and conducting a risk evaluation of a chemical substance.

D. EPA's asserted rationales in support of the pick-and-choose approach fail

1. The two statutory phrases EPA relies on do not grant it discretion to pick and choose

Neither of the two statutory phrases EPA plucks out of context grants it discretion to exclude conditions of use.

First, EPA's contention that the phrase "as determined by the Administrator" confers pick-and-choose authority is mistaken. *See* ER 4-5. This phrase merely confirms that EPA has a role in identifying the "circumstances" comprising a chemical's conditions of use under the statutory definition through factual investigation. *See* ER 4 (acknowledging that the "as determined by" phrase refers to a "largely … factual determination").

But EPA's role in "determin[ing]" the conditions of use is a limited one. The phrase "as determined by the Administrator" does not exist in a vacuum; the clause interrupts and modifies the rest of the definition. 15 U.S.C. § 2602(4). Thus, what EPA must "determine," i.e., identify by factual investigation, is bounded by the rest of the definition—the circumstances of a chemical's

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"intended, known, or reasonably foreseen" manufacture, processing, distribution, use, and disposal. *See id.* The phrase "as determined by" thus provides no authority for EPA to circumvent the statute's clear definition. *See U.S. Sugar Corp. v. EPA*, 830 F.3d 579, 631-32 (D.C. Cir. 2016) (rejecting reliance on statutory phrase "as determined by" to support "claim[ed] discretion"), *on reh'g en banc*, 671 F. App'x 822 (D.C. Cir. 2016), *and on reh'g en banc in part*, 671 F. App'x 824 (D.C. Cir. 2016).

Second, EPA cannot justify its pick-and-choose approach based on section 6(b)(4)(D), which requires EPA to "publish the scope of the risk evaluation …, including the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations the Administrator expects to consider." 15 U.S.C. § 2605(b)(4)(D). The phrase "expects to consider," understood in its ordinary meaning, does not provide discretion to pick and choose among the conditions of use. *See* Oxford American Dictionary 609 (3d ed. 2010) ("expect" means to "[r]egard (something) as likely to happen"); *supra* p. 27 (Congress used the word "discretion" when it meant to grant discretion). To the contrary, the term indicates only that EPA must describe the conditions of use it has identified through its fact-gathering. As EPA stated in the proposed rule, section 6(b)(4)(D) is "best read as directing the Agency to identify the uses and other activities that it has determined constitute the conditions of use, not as a license to choose among conditions of

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use." ER 64. If "expects to consider" were to grant EPA broad discretion to pick-and-choose and also modified all the preceding nouns, then EPA would also have broad discretion to exclude from the risk evaluation any hazards of the chemical (e.g., carcinogenic effects) that EPA chooses. But this interpretation is absurd.[7]

Moreover, contrary to EPA's assertions, TSCA's legislative history does not support the pick-and-choose approach. EPA relies heavily on a floor statement by a single senator to justify its interpretation, *see* ER 3, while ignoring a contradictory floor statement from four other senators, *see* 114 Cong. Rec. S3518-19 (daily ed. June 7, 2016). In light of the legislators' "contradictory account[s]," the statement of a single senator is not dispositive as to statutory meaning, especially when the statement is contrary to "clear statutory language." *NLRB v. SW Gen., Inc.*, 137 S. Ct. 929, 942-43 (2017); *Milner v. Dep't of Navy*, 562 U.S. 562, 572 (2011).

Even if TSCA were ambiguous, EPA's interpretation of the phrases "as determined by" and "expects to consider" as giving it carte blanche to exclude conditions of use is patently unreasonable. This is especially so because EPA's asserted discretion would be exercised even before conducting the evaluation that

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[7] Alternatively, under the rule of the last antecedent, the phrase "the Administrator expects to consider" does not even modify "conditions of use." *See Barnhart v. Thomas*, 540 U.S. 20, 26 (2003); *Nw. Forest Res. Council v. Glickman*, 82 F.3d 825, 832 (9th Cir. 1996), *as amended on denial of reh'g* (May 30, 1996).

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should answer how significant a risk the conditions of use actually present. If upheld, EPA's interpretation would give the Agency license to exclude *any* condition of use for *any* reason during (or even before) prioritization or risk evaluation. This irrational interpretation would undermine the integrity and protectiveness of those processes and cannot be squared with TSCA. Additionally, the pick-and-choose approach gives EPA license to implement TSCA in a manner wholly lacking in reasoned decision-making, rendering it arbitrary and capricious. *Cf. NRDC, Inc. v. EPA*, 863 F.2d at 1432.

2. EPA's view that it has unfettered discretion to exclude conditions of use is impermissible and lacks a rational basis

Implicitly conceding that Congress did not grant it unlimited discretion, EPA asserts that it intends to focus on evaluating "the conditions of use that raise greatest potential for risk." ER 3; *see* ER 180 (same); *see also* MA 17-18 (ACC handout urging EPA to limit risk evaluations to those conditions of use that "present the highest likelihood of potential concern"). EPA's non-binding intention cannot rescue the Framework Rules. First, no language in TSCA limits EPA to this "greatest potential for risk" focus. Nor does EPA point to any statutory terms that even arguably supply such a limitation.

Moreover, the Risk Evaluation Rule and the scopes for the first ten chemicals show that EPA intends to exclude conditions of use without any risk-based rationale (i.e., based on "nonrisk factors," *contra* 15 U.S.C. § 2605(b)(4)(A))

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and despite evidence that they do in fact present a serious potential for risk. For example, EPA indicates that it will exclude conditions of use of 1,4-dioxane when it is manufactured incidentally as a byproduct, a criterion with no connection to the level of risk presented, *see* 75 Fed. Reg. 49,656, 49,676 (proposed Aug. 13, 2010) (EPA "does not believe byproducts inherently pose lower exposures or risks than other manufactured chemical substances"), and that EPA itself has concluded falls within TSCA's jurisdiction, *see* 76 Fed. Reg. 50,816, 50,832 (Aug. 16, 2011). This exclusion of byproduct uses means that 1,4-dioxane's presence in many "commercial and consumer products," such as paints, household cleaners and detergents, and textile dyes, will not be evaluated, although these uses may present meaningful risks for some populations. MA 157, 170; ER 367; *cf.* ER 701. These excluded uses illustrate that EPA's "greatest potential for risk" rationale does not actually govern its exclusions.

In any event, focusing on only those conditions of use that EPA deems pose "the greatest potential for risk" is itself inconsistent with TSCA. The statute's plain terms require consideration of all conditions of use, not just the riskiest conditions. *See supra* pp. 23-26. There would be no way for EPA to determine soundly which conditions of use pose the greatest potential for risk *before* beginning the evaluation whose purpose is to assess the risks of those conditions of use. And it would be unreasonable to interpret the statute as allowing EPA to

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prioritize chemicals or conduct risk evaluations without considering risks from multiple (sometimes relatively low-dose) exposures to the same chemical. This exclusionary approach would prevent EPA from accurately evaluating total risks to vulnerable subpopulations like children, for whom low doses can pose significant risks, especially when they add up. *See supra* p. 32.

Likewise, EPA's "greatest potential for risk" theory is arbitrary and capricious because EPA has not provided a rational explanation to reconcile its pick-and-choose approach with TSCA's mandate to determine whether "a chemical substance" poses an unreasonable risk, including an unreasonable risk to vulnerable subpopulations, and to issue risk management rules to eliminate any such risks. *See State Farm*, 463 U.S. at 43.

Nor can EPA justify its pick-and-choose interpretation by reference to concerns about completing risk evaluations within "statutory deadlines." ER 3-4. This is not a legitimate excuse to disregard plain statutory language. *See Portland Gen. Elec. Co. v. Bonneville Power Admin.*, 501 F.3d 1009, 1026 (9th Cir. 2007). In any event, EPA has not explained its turnaround from its factual conclusion in the proposed Rule that including all conditions of use would be "manageable given the statutory deadlines." ER 64.

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II. EPA's use-by-use approach to risk determinations contravenes TSCA's requirement that EPA make a holistic risk determination for each chemical

EPA violates TSCA by asserting authority to determine the risk of individual conditions of use in isolation, not the chemical substance holistically. *See* 40 C.F.R. §§ 702.41(a)(9), 702.47, 702.49(d); ER 19. This aspect of the Risk Evaluation Rule flouts TSCA's command to determine whether "a chemical substance" presents an unreasonable risk, 15 U.S.C. § 2605(b)(4)(A), and defeats TSCA's purpose of preventing harms from toxic chemicals, *see supra* pp. 30-33. The holistic risk determination demanded by the statute must take into account that multiple exposures to the same chemical from different sources will increase risk. *See* 15 U.S.C. § 2605(b)(4)(F). If EPA considers each pathway to a chemical in isolation, as its Rule permits, it could determine that no single use poses an unreasonable risk, even where the totality of uses presents an unreasonable risk.

This use-by-use approach to risk determinations also cannot be squared with section 6(a), which requires EPA to issue a risk management rule if it determines that "any combination of" a chemical's "manufacture, processing, distribution in commerce, use, or disposal" presents an unreasonable risk. *Id.* § 2605(a). EPA cannot rule out the possibility that a combination of a chemical's conditions of use presents an unreasonable risk until after it has considered all of its conditions of use collectively. Sections 702.41(a)(9), 702.47, and 702.49(d) in the Risk

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Evaluation Rule are thus contrary to TSCA and must be set aside.

Under some circumstances EPA may determine that a particular use of a chemical *does* present an unreasonable risk before completing its risk determination. *See* 15 U.S.C. § 2605(a). This is because a "single use" may "present[] an unreasonable risk of injury for the population as a whole or for a susceptible subpopulation … regardless of the risk posed by other uses." ER 66. If EPA finds that a single use creates an unreasonable risk of harm, TSCA allows EPA to act quickly to protect public health, whether or not it has completed a risk determination for all uses, as EPA acknowledges. ER 15; *see* 15 U.S.C. § 2605(a), (b)(4)(A).

The converse, however, is not true. *See supra* pp. 30-33. Because the Risk Evaluation Rule allows EPA to determine that specific uses of a chemical do not pose an unreasonable risk before completing a comprehensive determination of the risks posed by the chemical, the Rule is contrary to law. *See Chevron*, 467 U.S. at 842-43.

III. EPA has unlawfully rewritten the statutory definition of "conditions of use" to omit certain uses and disposals

EPA rewrites Congress's unambiguous definition of "conditions of use" to significantly narrow the conditions of use the Agency will consider when making priority designations and conducting risk evaluations. ER 4, 5, 31. In contravention of the statutory definition, *see* 15 U.S.C. § 2602(4), EPA concludes

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that a chemical's ongoing use and disposal are *not* conditions of use if the chemical's manufacture, processing, or distribution for that specific use are not "prospective or on-going," ER 5. Moreover, EPA constricts the meaning of "disposal" to include only the one-time event when a chemical or product containing the chemical is placed in a landfill or other waste facility. Based on these contortions, EPA categorically omits from consideration three types of chemicals' conditions of use, which EPA misleadingly labels "legacy use," "associated disposal," and "legacy disposal." ER 4-5; *see* ER 31. This "rewriting [of TSCA's] unambiguous statutory terms" cannot stand. *Util. Air Regulatory Grp. v. EPA*, 134 S. Ct. 2427, 2445 (2014). Congress's clear definition controls the meaning of "conditions of use." *See Dig. Realty Tr., Inc. v. Somers*, 138 S. Ct. 767, 776 (2018); *United States v. Olson*, 856 F.3d 1216, 1223 (9th Cir. 2017).

A. A chemical's "conditions of use" include ongoing and future use and disposal under TSCA's plain language

TSCA's unambiguous text precludes EPA's conclusion that the term "conditions of use" ceases to apply to ongoing use and disposal once a chemical is no longer manufactured, processed, or distributed for a specific use. ER 4-5, 31. Although EPA asserts that TSCA is "ambiguous" and that "[n]o statutory text expressly addresses" the issue, ER 4, this is simply not so. A chemical's conditions of use include "the circumstances" under which the chemical is "known, or reasonably foreseen to be manufactured, processed, distributed in

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commerce, *used, or disposed of*." 15 U.S.C. § 2602(4) (emphasis added). Because the definition uses a disjunctive "or" list, each lifecycle stage of a chemical, standing alone, is a condition of use, even if some of the chemical's lifecycle stages have been discontinued. *See, e.g.*, *Horne v. Flores*, 557 U.S. 433, 454 (2009). EPA's construction robs the words "use" and "disposal" of their clear, independent role in the statute. The Court should reject EPA's attempt to "manufacture ambiguity" out of TSCA's plain language. *Aragon-Salazar v. Holder*, 769 F.3d 699, 706 (9th Cir. 2014).

Each of the three categories EPA concludes are *not* conditions of use falls squarely within the plain meaning of the definition. First, what EPA confusingly labels "legacy uses" includes ongoing and future uses of a chemical that is no longer manufactured, processed, or distributed for those specific uses. ER 4. Such uses are "circumstances" under which that chemical is "known" or "reasonably foreseen to be … used." 15 U.S.C. § 2602(4). For instance, notwithstanding that asbestos insulation is no longer produced in the United States, asbestos still insulates homes and buildings, is thus still *used* as insulation, and can become airborne if disturbed through remodeling or renovation. MA 111, 114-15; *see* 54 Fed. Reg. 29,460, 29,472-73 (July 12, 1989).

Second, so-called "associated disposal" refers to future disposals of a chemical relating to uses for which the chemical "is no longer manufactured,

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processed, or distributed." ER 4. This includes, for example, sending asbestos-containing debris from demolition of a building to a landfill. *See id.* Such disposals are "circumstances" under which a chemical is "known" or "reasonably foreseen to be … disposed of." 15 U.S.C. § 2602(4).

Third, so-called "legacy disposals" are "circumstances" under which a chemical is "known … to be … disposed of." *Id.* Contrary to EPA's assertion, these disposals are *ongoing*, not historical, activities. ER 4. "Disposal" of a chemical substance (including products containing that substance) is not a one-time occurrence when the substance or product is buried or placed in a landfill or other waste facility, but remains ongoing after the initial act of discard.

Although TSCA does not define "disposal," EPA previously defined the term in regulations implementing TSCA's requirement that EPA regulate disposal of a class of chemicals called polychlorinated biphenyls (PCBs). 15 U.S.C. § 2605(e); 40 C.F.R. § 761.3. EPA's regulations define disposal "very broadly to include any action that may be related to the ultimate disposition" of PCBs, including "accidental or intentional release of PCB[s] … to the environment." 43 Fed. Reg. 7150, 7150 (Feb. 17, 1978). EPA's "disposal" definition also includes "spills, leaks, and other uncontrolled discharges of PCBs as well as actions related to containing, transporting, destroying, degrading, decontaminating, or confining PCBs." 40 C.F.R. § 761.3. The ongoing activities of keeping the

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chemical "contain[ed] … or confin[ed]" are much broader than a one-time event. *Id.*

That disposal is not a one-time occurrence is also reflected in EPA's inclusion of "leaks, and other uncontrolled discharges" in its definition of disposal under TSCA. *Id.* Under EPA's regulations, disposal remains ongoing because PCB-contaminated soil can present ongoing and future risks if the substance leaks out of the containment or waste facility. *See In re Newell Recycling Co.*, 8 E.A.D. 598, TSCA Docket No. VI-659C (E.A.B. 1999), *aff'd*, *Newell Recycling Co. v. U.S. EPA*, 231 F.3d 204, 207-08 (5th Cir. 2000) (affirming EPA's rejection of claim that "PCB disposal is a one-time event"). For example, in *Environmental Defense Fund, Inc. v. EPA*, EPA acknowledged that PCB-containing "industrial waste and discarded end use products … in landfill sites … constitute[] a potential source of new free PCBs" that can be "a direct source of contamination for wildlife and humans." 636 F.2d 1267, 1270 (D.C. Cir. 1980) (quoting EPA Support Document).

In short, disposal of a chemical continues after it has been placed in a waste facility, and is a condition of use. 15 U.S.C. § 2602(4). The Court must set aside EPA's conclusion to the contrary.

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B. EPA's rewriting of the "conditions of use" definition is contrary to TSCA's structure and purpose

EPA's rewritten definition of "conditions of use" is inconsistent with the "overall statutory scheme" and purposes of TSCA. *See Brown & Williamson*, 529 U.S. at 133 (internal quotation marks omitted).

1. EPA's definition is at odds with TSCA's statutory scheme

First, EPA's interpretation ignores that when Congress amended section 6, it recognized that "inactive" chemicals could undergo prioritization and risk evaluation. As amended, section 8 of TSCA distinguishes between "active" chemicals, which had been manufactured or processed during the ten years prior to June 22, 2016, and "inactive" chemicals, which had not. 15 U.S.C. § 2607(b)(4)(A)(i)-(iii). In contrast, section 6 refers simply to "chemical substances," without reference to the date when the chemicals were last manufactured or processed. *Id.* § 2605. As the Senate Report accompanying an early version of the amended TSCA acknowledged, "there may be exposures of concern from substances that are not currently or no longer in commerce, and the section provides EPA authority to prioritize inactive substances that meet certain criteria." S. Rep. No. 114-67, at 11. The Court must presume that, by including the active/inactive distinction in section 8, but omitting the distinction in section 6, Congress acted intentionally. *See Russello v. United States*, 464 U.S. 16, 23 (1983). Thus, Congress intended EPA to prioritize, conduct risk evaluations on,

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and regulate chemicals with no recent manufacture or processing. Indeed, EPA itself rejected commenters' suggestion that EPA should not prioritize inactive chemicals. ER 32, 659. EPA's limited definition is at odds with Congress's deliberate scheme.

Second, EPA's interpretation would result in inconsistent treatment of identical activities based solely on whether manufacture or distribution is ongoing, a criterion that appears nowhere in section 6. For instance, under EPA's interpretation, a chemical's use in insulation constitutes a "condition of use" if the chemical is currently manufactured, processed, or distributed for use in insulation, but not otherwise. *See* ER 4; *compare* MA 229 (including as "condition of use" use of HBCD as insulation), *with* MA 114-115 (excluding from risk evaluation use of asbestos as insulation). This is so even if both uses present similar risks to public health. Omitting exposure scenarios from risk evaluations or prioritization decisions based on the happenstance of whether manufacturing, processing, or distribution for that specific use is ongoing is inconsistent with TSCA, as it involves considering a "nonrisk factor[]," just what TSCA prohibits. 15 U.S.C. § 2605(b)(1)(B), (b)(4)(A). These categorical omissions are capricious, in violation of TSCA.

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2. EPA's rewritten definition defeats TSCA's core purpose

EPA's three categorical omissions from the "conditions of use" definition, *see* ER 5, undermine TSCA's core aim to prevent unreasonable risks to health and the environment from toxic chemicals. *See* 15 U.S.C. §§ 2601(b), 2605(a)-(b). This statutory purpose is reflected both in the requirement that EPA regulate a chemical's use or disposal if either presents an unreasonable risk, and in EPA's broad authority to restrict "any manner or method" of a chemical's "use" or "disposal." *Id.* § 2605(a)(5)-(6). EPA's impermissible rewriting of the "conditions of use" definition will prevent it from making scientifically sound and health-protective decisions relating to priority designations and risk evaluations. Ongoing use and disposal of chemicals can pose significant risks that EPA must consider, even if the chemicals are no longer made, processed, or distributed for those uses.

EPA's ongoing risk evaluation of asbestos illustrates this point. Asbestos is no longer mined in the United States, few asbestos-containing products are still being imported, MA 111, and most asbestos-containing products are no longer being made, processed, or distributed. Yet large numbers of asbestos-containing products previously manufactured remain in use, including building materials such as insulation and flooring, and certain vehicle equipment. MA 114; *see also* MA 114-15 (identifying many discontinued asbestos-containing products with ongoing use and exposure, including floor tile, roofing felt, pipeline wrap, and more).

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Disposal of asbestos resulting from demolition, repair, or renovation of built structures or vehicle recycling is extensive, with disposal volumes totaling 25.6 million pounds in 2015. MA 116-17. Indeed, "the death rates from asbestos-caused diseases have remained constant," in part because of the "devastating health impact of asbestos in situ." ER 385. EPA's construction of "conditions of use" allows the Agency to ignore these health-threatening exposures in its risk evaluation. *See* MA 34 (Department of Health and Human Services urging EPA not to exclude "legacy uses" of asbestos, because such uses create "'new' hazardous exposure[s]" that pose significant risks to "fire fighters or building demolition [workers]").

Omitting ongoing use and disposal of chemicals no longer manufactured for those uses will also plague EPA's prioritization decisions. For example, when EPA considers whether to designate lead as high-priority, its analysis would be significantly under-inclusive if it omitted ongoing uses of lead-containing products—e.g., lead paint and lead-containing water pipes—that are no longer manufactured, but account for a substantial source of exposure to individuals. *See* 81 Fed. Reg. 60,304, 60,305 (proposed Sept. 1, 2016) (quoting CDC statement that "[l]ead-based paint and lead contaminated dust are the most hazardous sources of lead for U.S. children"); 56 Fed. Reg. 26,460, 26,470 (June 7, 1991) (contaminated drinking water contributes significantly to overall lead exposures); ER 699. EPA's

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erroneous omissions from lead's "conditions of use" would render its priority designation for lead grossly inadequate. Such omissions are at odds with the purposes of the 2016 TSCA amendments, which require consideration of populations with special vulnerabilities to chemicals, such as children.

C. EPA's contention that the "conditions of use" definition applies only prospectively is unreasonable

EPA's only justification for these categorical omissions is its specious contention that TSCA is "better interpreted to focus on the prospective flow of the chemical substance." ER 5.

First, as explained above, so-called legacy use, associated disposal, and legacy disposal are in fact ongoing and therefore prospective circumstances. *Supra* pp. 41-44.

Second, EPA's reliance on the passive infinitive phrase "to be" in the "conditions of use" definition is misguided. The definition plainly encompasses circumstances under which a chemical "is … *known* … to be … used, or disposed of." 15 U.S.C. § 2602(4) (emphasis added). The verb "to be" in this context describes a state of existence, i.e., that those circumstances of use and disposal are known to exist. For instance, lead pipes are "known to be used" in water distribution systems. This is true regardless of whether lead pipes continue to be manufactured or distributed.

Third, EPA's suggestion that it may have limited authority under TSCA to

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regulate use and disposal of discontinued products is both incorrect and irrelevant to the scope of risk evaluations conducted under section 6. ER 4. As discussed above, section 6(a) authorizes EPA to address risks from ongoing use and disposal of chemicals and products containing chemicals even in the absence of their ongoing manufacture, processing or distribution. 15 U.S.C. § 2605(a)(5)-(6).

Moreover, the possibility that EPA might identify an unreasonable risk that it lacks the tools to address, but that may be controlled by another agency, is not a valid reason to omit so-called legacy uses, associated disposal, and legacy disposal from risk evaluations and priority designations. TSCA section 9 expressly provides that, if EPA determines that a chemical presents an unreasonable risk that "may be prevented or reduced to a sufficient extent by action taken under a Federal law not administered by [EPA]," then EPA "shall" notify the other agency and ask whether the other agency will address the risk. *Id.* § 2608(a). The trigger for EPA to notify another agency under section 9(a) is a determination by EPA of unreasonable risk—a determination that can be made only *after* conducting a risk evaluation. *Id.* Congress thus anticipated that EPA's section 6(b) risk evaluations would include consideration of chemical exposures that may be most appropriately regulated by other agencies. EPA's approach would frustrate this deliberate statutory structure. *See supra* pp. 26-29.

Fourth, contrary to EPA's contention, *see* ER 5, the general presumption

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against construing a statute to be retroactive has no application to the question of statutory interpretation at issue. EPA's priority designations and risk evaluations do not "impair the rights a party possessed" in the past, "impose new duties with respect to transactions already completed," or impose any liability whatever. *See Landgraf v. USI Film Prods.*, 511 U.S. 244, 280 (1994).

In sum, considering the plain text of the "conditions of use" definition, the term's place in the statutory scheme, and TSCA's purposes, Congress unambiguously intended "conditions of use" to include ongoing and future uses and disposals of a chemical, even in the absence of ongoing manufacture, processing, and distribution for all or specific uses. EPA's categorical omission of so-called "legacy use," "associated disposal," and "legacy disposal" is unlawful and arbitrary. *See Chevron*, 467 U.S. at 842-43.

IV. The Framework Rules are inconsistent with EPA's obligation to base decisions on "reasonably available" information

TSCA requires EPA to consider all "reasonably available" information relating to a chemical when making prioritization decisions and conducting risk evaluations. 15 U.S.C. § 2625(k). The Framework Rules, however, preclude this consideration. The Prioritization Rule defines "reasonably available information" as "information that EPA possesses or can reasonably generate, obtain and synthesize for use, considering the deadlines … for prioritization and risk evaluation." 40 C.F.R. § 702.3; *id.* § 702.33 (same definition in Risk Evaluation

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Rule, but limited to risk evaluation deadlines). But the Rules include provisions that will prevent EPA from obtaining and developing the reasonably available information it needs—and is required to consider—to make legally and scientifically sound decisions under section 6. EPA also failed to consider how these provisions will inhibit its ability to develop needed information, "an important aspect of the problem." *State Farm*, 463 U.S. at 43.

A. The Risk Evaluation Rule will impermissibly chill the sharing of information by penalizing "incomplete" submissions by the public

Public participation plays a central role in EPA's efforts to obtain "reasonably available" information for risk evaluations. For example, EPA must provide notice of and allow public comment on draft risk evaluations. 15 U.S.C. § 2605(b)(4)(H); *see* 40 C.F.R. § 702.49(a). EPA also "encourage[s]" the public to provide comments and relevant information concerning manufacturers' requests for risk evaluations. 40 C.F.R. § 702.37(e)(4). Yet the Risk Evaluation Rule will deter public participation by placing commenters at peril of criminal punishment and civil penalties for submitting "incomplete" information. *Compare id.* § 702.31(d) (prohibiting "[s]ubmission to EPA of inaccurate, *incomplete*, or misleading information pursuant to a risk evaluation" (emphasis added)), *with* ER 73 (proposing penalties solely for incomplete submissions by manufacturers). This exceeds EPA's statutory authority and is unconstitutionally vague.

TSCA authorizes EPA to penalize only the "fail[ure] or refus[al] to comply

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with any requirement of [TSCA] or any rule promulgated, order issued, or consent agreement entered into" under the law. 15 U.S.C. § 2614(1). TSCA does not "require[]" members of the public to provide information to EPA. Thus, because 40 C.F.R. § 702.31(d) prohibits and threatens to penalize some voluntary information-sharing with EPA, it exceeds EPA's statutory authority and is invalid. *See City of Arlington v. FCC*, 569 U.S. 290, 297-98 (2013). It is also arbitrary and capricious for EPA to punish the public's submission of purportedly "incomplete" information, when the accumulated information EPA receives from individual commenters may well illustrate hazard or exposure patterns that would not come to light absent multiple submissions containing parts of the information. *Cf. NRDC, Inc. v. Pritzker*, 828 F.3d 1125, 1140 (9th Cir. 2016) (holding that agency acted contrary to law where it failed to consider how its choice to require "conclusive data" would result in underprotection of marine mammals by excluding potentially meaningful information).

In addition, by threatening members of the public with criminal and civil liability for providing incomplete information, section 702.31(d) runs afoul of the constitutional requirements of due process. A federal restriction violates due process protections when it is "so vague that it fails to give ordinary people fair notice of the conduct it punishes, or so standardless that it invites arbitrary enforcement." *Johnson v. United States*, 135 S. Ct. 2551, 2556 (2015). To

withstand scrutiny, section 702.31(d) requires the highest level of clarity because it touches on First Amendment activities of speech and petitioning the government, and subjects violators to criminal penalties. *Vill. of Hoffman Estates v. Flipside, Hoffman Estates, Inc.*, 455 U.S. 489, 498-99 (1982); *cf. Cal. Motor Transp. Co. v. Trucking Unlimited*, 404 U.S. 508, 510 (1972) (First Amendment protects petitioning).

Section 702.31(d) fails to meet this stringent standard. Members of the public and interested organizations, including Petitioners, would like to submit comments during EPA's TSCA risk evaluations. *Cf.* ER 442-80 (commenting on EPA's initial assessments under TSCA for three flame retardant clusters). But the Rule imposes criminal and civil liability for providing "incomplete" information, while providing no guidance regarding what would make a submission complete. That is unlawfully vague. *See State v. Mark Marks, P.A.*, 698 So. 2d 533, 534 (Fla. 1997) (statute criminalizing submission of "incomplete" demand letters is unconstitutionally vague for absence of guidance on meaning of "complete"); *cf. United States v. Crop Growers Corp.*, 954 F. Supp. 335, 345 (D.D.C. 1997) ("[W]here a statute or regulation imposes *no* duty whatever to disclose information, due process concerns require that criminal liability not be based on omission of such information." (citing *United States v. Murphy*, 809 F.2d 1427, 1431 (9th Cir. 1987))).

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The Rule's lack of clarity will not only subject individuals to arbitrary enforcement, it will "inevitably lead citizens to steer far wider of the unlawful zone … than if the boundaries of the forbidden areas were clearly marked." *See Grayned v. City of Rockford*, 408 U.S. 104, 109 (1972) (internal citations and quotation marks omitted). This chilling effect is unconstitutional. It will also undermine TSCA's intent by depriving EPA of information potentially relevant to its risk evaluations that would be "reasonably available," but for the vague threat of penalties.

Further, EPA did not consider the consequences of penalizing "incomplete" submissions, and did not even acknowledge that it had vastly expanded potential criminal liability as compared to the proposed rule. *See* ER 1-28. Imposing criminal and civil penalties without discussing these issues is arbitrary and capricious. *See Nat'l Parks Conservation Ass'n v. EPA*, 788 F.3d 1134, 1142-43 (9th Cir. 2015) (rejecting agency action where EPA did not "'cogently explain why it has exercised its discretion in a given manner'" (quoting *State Farm*, 463 U.S. at 48)).

B. The Framework Rules impermissibly use the factors in TSCA section 26(h) to screen, rather than weigh, information

The Risk Evaluation Rule also violates TSCA by limiting the information manufacturers must submit when requesting a risk evaluation to "[s]cientific information [that is] consistent with the scientific standards in 15 U.S.C. 2625(h)."

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40 C.F.R. § 702.37(b)(6). Section 26(h) requires that when EPA makes "a decision based on science," it must "consider as applicable" five factors to guide its decisions about the reliability of information. 15 U.S.C. § 2625(h). These factors include "the extent to which the information is relevant for [EPA's] use in making a decision about a chemical"; the "degree of clarity and completeness" with which the underlying data and analyses are documented; and "the extent to which the variability and uncertainty in the information … are evaluated and characterized." *Id.*

Section 702.37(b)(6) violates TSCA. It is both inconsistent with section 26(h) and contrary to section 26(k)'s mandate that EPA consider "reasonably available" information. *See* 15 U.S.C. § 2625(k).

First, section 702.37(b) impermissibly converts the section 26(h) considerations *EPA* must apply when weighing information into threshold requirements *manufacturers* must use to screen and limit the information they are permitted to submit to EPA. Nothing in the plain text of section 26(h) indicates that the factors are bright-line criteria for withholding information from EPA. To the contrary, each factor includes the phrase "degree of" or "extent to which," without identifying any threshold that would be disqualifying. This shows that Congress intended these factors to help EPA assess the weight information should be given based on its relative scientific reliability, not to create minimum

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thresholds of reliability below which information must be withheld from EPA altogether. *Cf.* 15 U.S.C. § 2625(i) (directing EPA to make decisions "based on the weight of the scientific evidence"). EPA's conversion of these weight-of-the-evidence factors into a screening tool defies Congress's unambiguous intent.

Second, directing manufacturers to withhold information *the manufacturer decides* is not "consistent with" section 26(h) will prevent EPA from considering information relating to the chemical that is "reasonably available," in violation of section 26(k). For example, a manufacturer could decide that the documentation of "data, assumptions, … and analyses employed to generate the information" does not rise to the "degree of clarity and completeness," *id.* § 2625(h)(3), that makes it subject to disclosure under the Rule, 40 C.F.R. § 702.37(b)(6).[8] The withheld data, even if less than perfectly clear or complete, might have added to EPA's body of knowledge about the chemical. For this reason, section 702.37(b)(6) violates section 26(k)'s mandate that EPA consider reasonably available information. *Cf. Pritzker*, 828 F.3d at 1140 (rejecting agency's decision to rely on "screening criteria" that required "conclusive data" where such data were extremely difficult to obtain).

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[8] EPA provided no discernible standards for what it would mean for information to be "consistent with" "the degree of clarity" or any of these other weighing factors.

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The Prioritization Rule similarly incorporates an unlawful information screen. It states that during the prioritization process, EPA "expects to consider sources of information … consistent with the scientific standards in [section 26(h)]." 40 C.F.R. § 702.9(b). Just as EPA violated TSCA by directing manufacturers to withhold information that does not meet the section 26(h) "standards," EPA violated TSCA by erecting a "screen" that excludes some reasonably available information from EPA's prioritization process—rather than allowing EPA to weigh that information.

C. The Risk Evaluation Rule unlawfully and arbitrarily permits manufacturers to determine what information is relevant when requesting a risk evaluation

The Risk Evaluation Rule permits a manufacturer to withhold information critical to EPA's comprehensive evaluation of a chemical, if the manufacturer decides the information is not relevant to the specific conditions of use it is asking EPA to evaluate. Under the Rule, manufacturers must submit only "information that is relevant to whether the chemical substance, under the circumstances *identified by the manufacturer(s)*, presents an unreasonable risk." 40 C.F.R. § 702.37(b)(4) (emphasis added). This provision is contrary to TSCA and arbitrary and capricious.

To the extent the Rule allows EPA to limit risk evaluations to the conditions of use in the manufacturer's request, it rests on a faulty legal premise. As shown

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above, risk evaluations must address all of a chemical's conditions of use. *See supra* pp. 23-26. Without information on all conditions of use, EPA cannot conduct a full evaluation.

Allowing manufacturers to withhold information about chemicals also flouts the requirement that EPA base the requested risk evaluations on "reasonably available" information. 15 U.S.C. § 2625(k). Relevant information about a chemical's conditions of use in the manufacturer's possession is plainly "reasonably available." *Id.* Consistent with the proposed rule, ER 74, EPA must require manufacturers requesting risk evaluations to submit all such relevant information for all of a chemical's conditions of use.

The Rule is also arbitrary and capricious, for two reasons. First, EPA has given no justification for its choice to allow manufacturers to withhold information in their possession relevant to EPA's risk evaluations. *See Arrington v. Daniels*, 516 F.3d 1106, 1114 (9th Cir. 2008). Second, it is irrational to allow manufacturers to withhold relevant and reasonably available information from their risk evaluation requests, while requiring general public commenters to provide "complete" information or risk civil and criminal penalties. *See supra* pp. 52-55.

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D. EPA must consider during prioritization whether it has adequate information to conduct a risk evaluation

The Prioritization Rule does not require EPA to consider during the prioritization process whether it has adequate information about a chemical to conduct a risk evaluation; rather, EPA will consider only whether it has sufficient information "for purposes of prioritization" alone. 40 C.F.R. § 702.5(e); *see id.* § 702.5(b) (similar).[9] This limitation cannot be reconciled with the "reasonably available information" requirement. *See* 15 U.S.C. § 2625(k). By EPA's own definition, "reasonably available information" includes information EPA "possesses or can reasonably generate … considering [TSCA's] deadlines for prioritization *and risk evaluation*. 40 C.F.R. § 702.3 (emphasis added). Given this plain language, EPA's failure to consider what information it will need for risk evaluation during the prioritization phase violates TSCA and is arbitrary and capricious.

As a practical matter, it is important that EPA consider the information it needs for risk evaluation before beginning the prioritization process for a chemical. TSCA requires EPA to designate a chemical as low- or high-priority within twelve months of beginning the prioritization process, 15 U.S.C. § 2605(b)(1)(C). A high-

[9] In contrast, under the proposed rule EPA would have considered what information it needed for *both* prioritization and risk evaluation during the prioritization process. *See* ER 587.

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priority designation triggers further statutory deadlines for completing the risk evaluation. *See id.* § 2605(b)(3)(A), (b)(4)(G).

As EPA acknowledged in the proposed Rule, these deadlines may be too short for EPA to obtain needed information if it does not start gathering information before the risk evaluation commences. ER 583 ("EPA cannot assume that it will be able to require the generation of critical information during these time frames. … Tests necessary for risk evaluation, for example, could take months or years to develop and execute."). Analyzing certain hazards—such as developmental effects, neurotoxicity, and reproductive toxicity—typically requires longer-term testing; such information is particularly crucial to evaluate risks to vulnerable subpopulations such as infants, children, and pregnant women. *See* MA 653-56; *supra* p. 32; *cf.* ER 33 (noting that EPA may "need" to require "longer-term testing … to more completely consider the hazard characteristics and exposure pathways of a chemical").

Given the intertwined deadlines for prioritization and risk evaluation, if EPA does not consider the availability of information for risk evaluation before prioritization, EPA may be unable to obtain all "reasonably available" information that Congress required it to consider within the statutory timeframes. *See* 15 U.S.C. § 2625(k). This violates TSCA.

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V. Petitioners have standing

A. Petitioners have standing to bring this case on behalf of their members

Petitioners[10] have standing to challenge the Framework Rules on behalf of their members under the three-part test established in *Hunt v. Washington State Apple Advertising Commission*, 432 U.S. 333, 343 (1977). First, protecting their members from exposures to toxic chemicals is central to Petitioners' purposes. *E.g.*, PA 5-6, 43-45, 77-78, 206-11, 263-66, 384-86, 394-98, 424-29. Second, neither adjudication of the legal claims at issue nor the relief requested requires individual members' participation. *See Hunt*, 432 U.S. at 342-43.

Third, Petitioners' members would have standing to sue on their own behalf: EPA's unlawful approach to prioritization and risk evaluation injures the members by increasing the risk that they will suffer harm from exposure to toxic chemicals. *See NRDC, Inc. v. U.S. EPA*, 735 F.3d 873, 878-79 (9th Cir. 2013) (finding standing where organization showed a "credible threat" that members' children would be exposed to dangerous pesticide registered by EPA); *Cent. Delta Water Agency v. United States*, 306 F.3d 938, 948 (9th Cir. 2002) ("threat of injury" to

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[10] The membership-based Petitioners are: Alaska Community Action on Toxics, Alliance of Nurses for Healthy Environments, Cape Fear River Watch, Environmental Defense Fund, Environmental Health Strategy Center, Learning Disabilities Association of America, Natural Resources Defense Council, Sierra Club, Vermont Public Interest Research Group, United Steelworkers, and WE ACT for Environmental Justice.

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plaintiffs' crops from agency's planned water release schedule confers standing); *Hall v. Norton*, 266 F.3d 969, 976 (9th Cir. 2001).

1. Threat of harm from Risk Evaluation Rule

Petitioners' members experience a credible threat of health harms from ongoing exposure to chemicals that EPA is currently evaluating pursuant to the Risk Evaluation Rule, including asbestos, 1,4-dioxane, PERC, TCE, and HBCD. There is no doubt that Petitioners' members are exposed to these chemicals. *See, e.g.*, PA 200-03, 247-48, 294-96, 332-34. United Steelworkers' members, for instance, are exposed to asbestos when they repair, maintain, or replace equipment with asbestos-containing gaskets or insulation, and through the manufacture of chlorine and caustic soda in chlor-alkali plants. PA 387-88; *see* PA 518-23, 643-45. Cape Fear River Watch has members whose drinking water comes from a river with some of the highest documented levels of 1,4-dioxane contamination in the country, contamination that is not fully removed through water treatment. PA 62, 74; *see* PA 544-47. Alaska Community Action on Toxics' members are exposed to HBCD, which bio-magnifies in the arctic animals and fish that make up integral components of their diets. PA 15-18. The serious adverse health effects of each of these chemicals, even at low levels of exposure, are well established. PA 526, 616-21, 656-57, 680-83, 859-62.

These members face a credible threat, and reasonably fear, *NRDC v. U.S.*

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EPA, 735 F.3d at 878, that the flaws in EPA's Risk Evaluation Rule—e.g., exclusion of known or foreseeable exposures from risk evaluations, failure to make holistic risk determinations, deterring submission of all "reasonably available information"—will lead EPA to understate the risks posed by chemicals undergoing review. *See, e.g.*, MA 114-15 (excluding *in situ* uses of asbestos), 170 (excluding uses of 1,4-dioxane as a byproduct and impurity). If EPA understates risk, Petitioners' members will receive less protection than if the Rule complied with TSCA. *See, e.g.*, PA 18-23, 82-83, 212-15, 249, 273-76, 300-01, 329, 334, 387-91, 398-404. Although members attempt to remain vigilant to minimize their exposure, and incur costs to do so, they cannot completely avoid exposure to these chemicals. PA 39-40, 255-57, 291, 295-97, 332-33.

EPA's unlawful evaluation process thus threatens to increase the risk of members' exposure to chemicals like asbestos, HBCD, 1,4-dioxane, TCE, and PERC. These are exactly the types of risks Congress sought to reduce through TSCA, *see* 15 U.S.C. § 2601(b); *supra* pp. 6, 8, which "reinforc[es]" the conclusion that these injuries are cognizable for purposes of standing. *Baur v. Veneman*, 352 F.3d 625, 635 (2d Cir. 2003); *see also Covington v. Jefferson Cty.*, 358 F.3d 626, 638 (9th Cir. 2004).

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2. Threat of harm from Prioritization Rule

Petitioners' members are also reasonably concerned about the risks to their health from exposure to lead, a chemical not yet designated as high-priority, but included in the 2014 Workplan list of chemicals from which TSCA directs EPA to select high-priority chemicals. *See* ER 371. For example, members have credible concerns about their or their children's ongoing lead exposure through drinking water, household dust, and in occupational settings. PA 39-41, 251-53, 256-58, 325-29, 390-91, 420-22.

The cumulative, irreversible damage lead wreaks on the developing brains of children is undisputed. *See In re A Cmty. Voice*, 878 F.3d 779, 787 (9th Cir. 2017); PA 440-44. Especially at low levels of exposure, each additional exposure to lead can contribute to harming children's health. *See* PA 443. Adult lead exposure is also associated with adverse health outcomes. PA 444-45.

Because the Prioritization Rule allows EPA to omit conditions of use, including known, ongoing uses of lead, from its screening review, *see supra* pp. 42, 48-49; ER 31, EPA's designation of lead as high- or low-priority will not account for the full potential risk from lead. As a result, EPA's decision about whether lead "may present an unreasonable risk," including to vulnerable subpopulations like children and workers, will not conform to statutory requirements. *See* PA 277-82, 390-91, 433-34. If lead is not designated as high-

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priority, then EPA will not conduct an evaluation to determine whether lead presents an unreasonable risk that requires risk management under TSCA. Petitioners' members thus have reasonable concerns that if no risk evaluation is conducted for lead, they and their children will face an increased risk of ongoing harmful exposure.

Similarly, Petitioners' members are exposed to a variety of flame retardant chemicals, including polybrominated diphenyl ethers (PBDEs). PA 10, 80-83, 415-16. PBDEs are associated with cognitive and developmental harms in children. *See* PA 84-85, 268, 285-86. Several PBDEs are no longer produced or imported, but are still present in homes from so-called legacy uses. PA 83. Under the Prioritization Rule, EPA will ignore those uses and resulting exposures, and thus is more likely to designate these chemicals as low-priority despite PBDEs' well-recognized hazard and exposures.

3. These harms are traceable to the Framework Rules and redressable

Under the "relaxed" standards applicable here, these members' procedural injuries are traceable to the Framework Rules and will likely be redressed by a favorable decision by this Court. *See Cottonwood Envtl. Law Ctr. v. U.S. Forest Serv.*, 789 F.3d 1075, 1083 (9th Cir. 2015). Petitioners seek to enforce a statutorily required process for evaluating chemical risks, "the disregard of which could impair" their members' "separate concrete interest" in minimizing their exposure

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to harmful chemicals. *See Or. Nat. Desert Ass'n v. Dombeck*, 172 F.3d 1092, 1094 (9th Cir. 1998) (quoting *Lujan v. Defs. of Wildlife*, 504 U.S. 555, 572 (1992)); *see also Salmon River Concerned Citizens v. Robertson*, 32 F.3d 1346, 1355 (9th Cir. 1994) (finding causation and redressability where agency's deficient environmental analysis might cause environmental and health consequences to be overlooked).

A favorable decision by this Court would redress this injury, because it would compel EPA to assess chemical risks comprehensively, thereby requiring EPA to accurately determine whether a chemical presents an unreasonable risk and issue protective rules to eliminate any such risk. *See Idaho Conservation League v. Mumma*, 956 F.2d 1508, 1517-18 (9th Cir. 1992) (finding redressability where plaintiffs alleged that agency's failure to follow statutorily required procedures caused it not to recommend protecting wilderness areas, thereby opening the areas to future development); *see also N.Y. Pub. Interest Research Grp. v. Whitman*, 321 F.3d 316, 325-26 (2d Cir. 2003) (finding redressability where plaintiffs averred that Clean Air Act violations created uncertainties about whether plaintiffs were being exposed to harmful air pollution).

B. Petitioners have organizational and informational standing to challenge the Risk Evaluation Rule

Petitioners Environmental Working Group, Union of Concerned Scientists, Safer Chemicals Healthy Families, and Asbestos Disease Awareness Organization

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have standing because the organizations have suffered "both a diversion of [their] resources and frustration of [their] mission[s]." *Fair Housing Council of San Fernando Valley v. Roommate.com, LLC*, 666 F.3d 1216, 1219 (9th Cir. 2012) (internal quotation marks omitted). These organizations' missions will be frustrated by the Risk Evaluation Rule insofar as a core part of their work is providing their constituencies with accurate information about chemicals to which they are exposed. PA 52-54, 60, 229-31, 307; *see also* PA 364-65 (explaining that mission includes ensuring member-scientists have access to data). In this work, the groups and their members rely extensively on government information about the uses and health risks of chemicals, including information TSCA requires EPA to release. PA 59-60, 225, 344-47; 15 U.S.C. § 2605(b)(4)(C) (requiring EPA to "publish" final risk evaluations). TSCA aims to develop "adequate information" about the effects of chemicals on health and the environment, 15 U.S.C. § 2601(b)(1), and to "increase access" to that information, H.R. Rep. No. 114-176, at 16.

Because the Risk Evaluation Rule unlawfully allows EPA to exclude conditions of use and ignore the combined exposure from multiple uses of a chemical, the information it publishes concerning a chemical's "hazards and exposures" will be incomplete. *See* 15 U.S.C. § 2605(b)(4)(F)(i). This will frustrate these Petitioners' missions of creating and distributing accurate,

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comprehensive educational materials about chemical risks.

Instead of relying on EPA, the groups and their members will be forced to "expend additional resources that they would not otherwise have expended" on new research and data collection to close gaps in the government's data. *See* PA 230-31, 345-47. These injuries give rise to organizational standing. *See Nat'l Council of La Raza v. Cegavske*, 800 F.3d 1032, 1040 (9th Cir. 2015); *Am. Canoe Ass'n v. City of Louisa Water & Sewer Comm'n,* 389 F.3d 536, 544-47 (6th Cir. 2004); *Fair Housing Council*, 666 F.3d at 1219.

In addition, the Risk Evaluation Rule will prevent Petitioners and their members from "obtain[ing] information which must be publicly disclosed pursuant to the statute." *See Fed. Election Comm'n v. Akins*, 524 U.S. 11, 20-21 (1998); PA 21, 59-60, 75, 223-28, 281-82, 343-47, 385, 400-01. This informational injury also gives rise to standing. *See Friends of Animals v. Jewell*, 824 F.3d 1033, 1041 (D.C. Cir. 2016).

CONCLUSION

Petitioners respectfully request that this Court grant the petitions for review and set aside these rules "in part." 15 U.S.C. § 2618(c)(2). Vacatur, along with remand, is the presumptively appropriate remedy here. *See Cal. Wilderness Coal. v. U.S. Dep't of Energy*, 631 F.3d 1072, 1095 (9th Cir. 2011). Petitioners request that the Court vacate and remand the following provisions of the Framework

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Rules: 40 C.F.R. §§ 702.5(b), (e), 702.7(a), 702.9(b)-(c), (f), 702.31(d), 702.37, 702.41(a)(5), (a)(7)-(9), (b)(2), (c)(1), (c)(4)(i), (c)(4)(iii), (d)(2), 702.43(a)(1), 702.47, 702.49(b)(1), (c), (d), and the following portions of the preambles: Prioritization, IV.B (ER 31), IV.J (ER 34-34), and Risk Evaluation, III.B (ER 3-6), III.G (ER 10-13), III.H.1.d-e (ER 14-15), III.H.2 (ER 15-16), III.I.1 (ER 16), and III.I.6 (ER 19). Petitioners also respectfully request that the Court issue declaratory relief that TSCA requires priority designations and risk evaluations to consider all circumstances within the statutory definition of conditions of use.

April 16, 2018

Respectfully submitted,

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STATEMENT OF RELATED CASES

Petitioners are unaware of any related cases within the definition of Circuit Rule 28-2.6.

Dated: April 16, 2018

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CERTIFICATE OF COMPLIANCE

This brief complies with the type-volume limitation of Fed. R. App. P. 32(a)(7)(B) because it contains 15,332 words, excluding the parts of the brief exempted by Fed. R. App. P. 32(a)(7)(B)(iii). This brief complies with the typeface requirements of Fed. R. App. P. 32(a)(5) and the type style requirements of Fed. R. App. P. 32(a)(6) because it has been prepared in a proportionally spaced typeface using Microsoft Office Word 2016 and 14-point Times New Roman font.

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CERTIFICATE OF SERVICE

I hereby certify that I electronically filed the foregoing with the Clerk of the Court for the United States Court of Appeals for the Ninth Circuit by using the appellate CM/ECF system on April 16, 2018.

I certify that all participants in the case are registered CM/ECF users and that service will be accomplished by the appellate CM/ECF system.

Dated: April 16, 2018

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Exhibit 2

IN THE UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

SAFER CHEMICALS, HEALTHY FAMILIES et al., *Petitioners,* v. U.S. ENVIRONMENTAL PROTECTION AGENCY et al., *Respondents.* IPC INTERNATIONAL, INC. et al., *Respondents-Intervenors.*	Docket No. 17-72260 Consolidated with Docket Nos. 17-72501, 17-72968, 17-73290, 17-73383, 17-73390

DECLARATION OF PATRICIA D. KOMAN, PH.D., M.P.P.
IN SUPPORT OF PETITIONERS' OPENING BRIEF

I, PATRICIA D. KOMAN, do hereby affirm and state:

Introduction and Qualifications

1. I am a Research Investigator and Scientist at the University of Michigan School of Public Health, Environmental Health Sciences Department. In that role, I am responsible for conducting scientific research regarding how environmental contaminants affect human health. I am also the President and Senior Health Scientist at Green Barn Research Associates, Ann Arbor, Michigan. As a public health professional, I apply my scientific methods to study the effects of environmental and social factors on health.

2. I earned a Ph.D. (2016) in Environmental Health Sciences from the University of Michigan, School of Public Health, in Ann Arbor, Michigan. I earned a masters degree in public policy (1994) from the University of California at Berkeley. I earned a bachelors of arts with distinction, *Phi Beta Kappa* (1988), from the University of Virginia, Charlottesville, Virginia.

3. I have worked at the University of Michigan as a scientist since 2012. My work at the university is focused on the link between chemicals in our environment—including air pollutants, water contaminants, and consumer and industrial products—and human health, with a particular emphasis on vulnerable populations.

4. Previously, for 22 years, I served as a senior environmental scientist and program manager at the U.S. Environmental Protection Agency (EPA). There I conducted risk assessments and evaluated scientific literature about how the environment affects health from a variety of sources. I was awarded the Administrator's Award for Excellence for my health impact assessments and methodological advances. I have authored government reports with peer-reviewed methodologies. I earned four Gold Medals for exceptional service.

5. I have published articles in peer-reviewed scientific journals, including articles on the identification of vulnerable populations for protection from harm through health-based standards. I have authored numerous government

reports, such as Reports to Congress, *Federal Register* notices, staff summaries of scientific data (staff paper) and regulatory impact assessments.

6. I have presented testimony and comments to state and federal agencies on the regulation of toxic chemicals. I have organized and participated as an expert in educational programs with experts on chemical policy (including 1,4-dioxane) at the University of Michigan and the American Public Health Association annual meeting.

7. I have been invited by the State of Michigan Department of Environmental Quality to provide scientific input on hazardous chemical clean-up criteria and lead in drinking water issues related to the Flint water crisis. I managed an environmental educational program regarding water quality, with over 1,000 contacts with Flint residents and middle school students.

8. A more complete description of my educational and work experience, as well as a complete list of my publications, is attached to this declaration as Exhibit A.

9. By virtue of my training, experience, and knowledge of the pertinent scientific literature, I am considered by my peers as an expert in the public health impacts and sources of exposure to 1,4-dioxane.

10. All of the information set forth in this declaration is based upon my education, personal knowledge, experience, and my personal review of the

pertinent literature, including the documents listed as references at the end of this declaration.

Sources and Uses of 1,4-Dioxane (CASRN: 123-91-1)

11. 1,4-Dioxane is a chemical that contains four carbon atoms and two oxygen atoms in a ring.

12. 1,4-Dioxane is an industrial solvent manufactured in large quantities (up to 10 million lbs/year) for numerous industrial, commercial, and consumer uses. (Agency for Toxic Substances and Disease Registry 2012; Integrated Risk Information System 2013). In industrial use, 1,4-dioxane is a byproduct (a chemical formed as an incidental result) in manufacturing processes involving ethylene oxide, such as the production of the common plastic polyethylene terephthalate (PET), polyester, and ethyoxylated surfactants. The hazards posed by 1,4-dioxane are identical whether it is produced intentionally or as a byproduct.

13. 1,4-Dioxane is used as both a laboratory reagent and as an ingredient in the manufacture of a second industrial chemical (e.g., as an intermediate, an extraction medium for fats and oils, and as part of a polymerization catalyst that speeds up a chemical reaction). 1,4-Dioxane is also used in a wide variety of commercial and consumer products, including personal care products, detergents, waxes, and antifreeze. Other uses of 1,4-dioxane documented in Europe include commercial and consumer products such as lacquers, varnishes, paint strippers,

dyes, greases, cleaners and detergents, adhesives, cosmetics and deodorants (ECJRC 2002).

14. 1,4-Dioxane is also present as a contaminant in cosmetics, detergents, shampoos, pharmaceuticals, foods, agricultural and veterinary products and ethylene glycol-based antifreeze coolants, because it is a byproduct of manufacturing involving ethylene oxide (Agency for Toxic Substances and Disease Registry 2012). Although in the U.S. many manufacturers remove 1,4-dioxane through vacuum stripping in consumer cosmetics and household products, the U.S. Food and Drug Administration has stated 1,4-dioxane is still present in significant amounts in some products (ATSDR, 2012). In addition, tests conducted by the Campaign for Safe Cosmetics document concentrations of 1,4-dioxane in children's and adult bath products (Campaign for Safe Cosmetics, 2007). Products found to contain 1,4-dioxane include shampoo, conditioner, liquid hand soap, body wash, skin moisturizer, and baby lotion (Environment Canada, 2010).

15. The use and disposal of 1,4-dioxane in the past has led to environmental contamination that is contributing to ongoing exposures. Because 1,4-dioxane had been widely used as a stabilizer in certain chlorinated solvents, 1,4-dioxane is frequently found within groundwater contaminated with chlorinated solvents (Adamson et al. 2014; Knappe, D. Lopez-Velandia, C. Hopkins, Z. Sun 2016).

16. As of 2016, 1,4-dioxane had been identified at more than 34 sites on the EPA National Priorities List, the list of hazardous waste sites eligible for remediation under the federal Superfund program; it may be present (but samples were not analyzed for it) at many other sites (EPA 2016b).

17. These uses described in Paragraphs 12 through 16 above have led to widespread 1,4-dioxane exposure in the United States.

Environmental Fate and Transport

18. 1,4-Dioxane dissolves quickly and easily in water and is persistent. 1,4-Dioxane leaches readily from soil to groundwater, is miscible in water (meaning it dissolves completely), migrates rapidly in groundwater. In groundwater, 1,4-dioxane forms the leading edge of a pollution plume and travels much faster, farther, and more widely than other volatile organic compounds. Thus, 1,4-dioxane can rapidly reach drinking water or enter house basements through soil or groundwater intrusion, for example, contributing to exposures often before other pollutants are detected.

19. 1,4-Dioxane has been used at many industrial and federal facilities like military bases because of its widespread utility with other solvents.

20. Improper disposal or storage has caused 1,4-dioxane spills at military, defense contracting, and other industrial facilities (Integrated Risk Information

System 2013). Based on this history, unintentional releases and spills are reasonably foreseeable wherever the chemical is widely used.

Human Exposure to 1,4-Dioxane

21. As described below, human exposure to 1,4-dioxane is widespread as a result of its wide variety of uses. People come into contact with this substance through: drinking water, personal care products, household products, cosmetics, and occupational exposures, among other sources.

22. In the United States, humans are exposed to 1,4-dioxane primarily through ingestion of contaminated water and food and dermal contact with consumer products (Agency for Toxic Substances and Disease Registry 2012; ECJRC 2002; DHHS 2017).

23. Worker exposures include inhalation of vapors, skin absorption, ingestion, and skin and/or eye contact (Agency for Toxic Substances and Disease Registry 2012; ECJRC 2002; DHHS 2017; NIOSH 2010). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 430,000 workers, including 149,697 women, potentially were exposed to 1,4-dioxane (Boiano and Hull 2001; NIOSH 1990). Exposures occur during the production and use of 1,4-dioxane as a stabilizer or solvent (Agency for Toxic Substances and Disease Registry 2012; ECJRC 2002; DHHS 2017).

24. Exposures of 1,4-dioxane via drinking water are widespread and are documented back to the 1980s (Dietrich, A.M., D.S. Millington 1983; Stanton 2016; MDEQ 2018).

25. According to EPA's Toxic Release Inventory for 2014, 96,437 pounds of 1,4-dioxane were released to the air, 24,262 to surface water, and 422,943 pounds were transferred from the facility for off-site disposal (US EPA TRI Explorer, Release Chemical Report database, available at https://iaspub.epa.gov/triexplorer/tri_release.chemical). Total annual environmental releases of 1,4-dioxane reported by EPA's Toxics Release Inventory from 1988 to 2009 ranged from 0.3 million to 1.3 million pounds (DHHS 2017).

26. Based on drinking water sampling conducted under the direction of EPA, a significant portion of the municipal drinking water systems in the United States have 1,4-dioxane at levels associated with increased risk of serious health problems. Specifically, 2017 results from EPA's Third Unregulated Contaminant Monitoring Rule (UCMR3 at https://www.epa.gov/sites/production/files/2017-02/documents/ucmr3-data-summary-january-2017.pdf) indicate that over 6.9% of 4,905 public drinking water systems serving >10,000 people had concentrations of 1,4-dioxane above the EPA Reference Concentration of 35 micrograms/L, which signifies these populations could be likely to experience appreciable risk of deleterious effects (US

Environmental Protection Agency 2009; Integrated Risk Information System 2013).

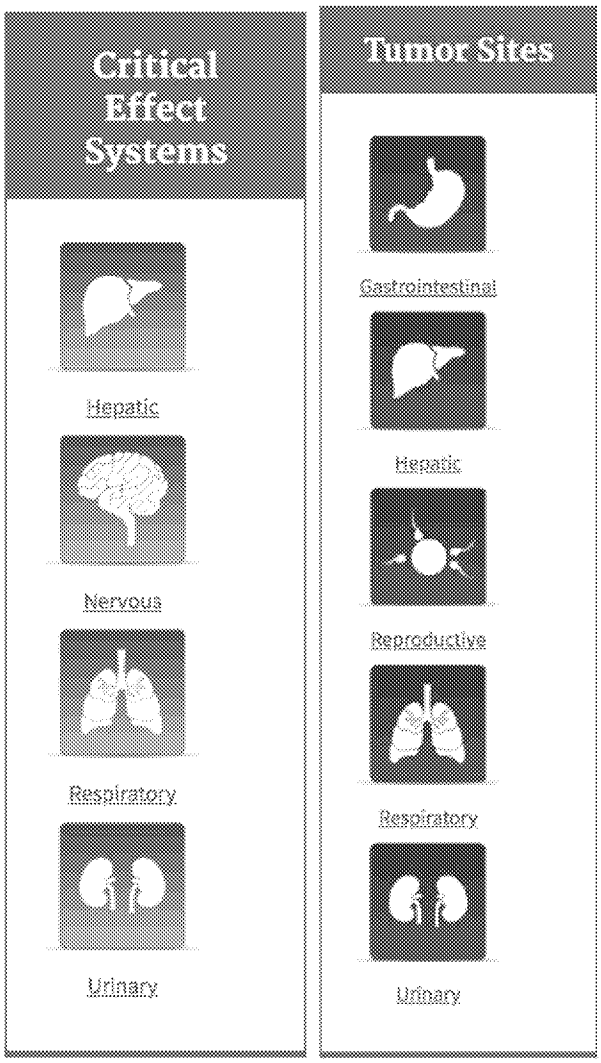
27. The EPA testing omits small public drinking water systems (i.e., systems serving <10,000 people), which account for about 27% of the U.S. Population (US Environmental Protection Agency 2017). Private wells are also not included in EPA's testing. Therefore, the UCMR3 results underestimate potential exposures (Sun, Lopez-Velandia, and Knappe 2016).

28. 1,4-Dioxane is present in a wide variety of consumer products, including household detergents, cosmetics/ toiletries, and foods (Integrated Risk Information System 2013). Based on an analysis of the ingredients in 15,000 cosmetic and other personal-care products, 22% of all such products may contain 1,4-dioxane (EWG 2017). Dermal contact is a relevant route of exposure. Cosmetics and personal care products have the potential to contribute significantly to exposures, since people are applying them directly to their bodies, often multiple times per day, every day (DHHS 2017).

Human Health Effects of 1,4-Dioxane

29. As described below, 1,4-dioxane is readily absorbable; distributes rapidly through the body, is likely to cause cancer in humans by all routes of exposure; and is associated with adverse reproductive effects. Long-term exposure to 1,4-dioxane may cause kidney and liver damage. Short-term exposure to high

levels of 1,4-dioxane may result in nausea, drowsiness, headache, and irritation of the eyes, nose and throat. The graphic below taken from the IRIS program summarizes for 1,4-dioxane exposure the four critical effect systems and the five tumor sites.



Summary of Critical Effect System and Tumor Sites for 1,4-Dioxane Exposure

Source: US EPA IRIS Program 2013

30. 1,4-Dioxane is readily absorbed through the lungs and gastrointestinal tract (Integrated Risk Information System 2013).

31. Distribution is rapid and uniform in the lung, liver, kidney, spleen, colon and skeletal muscle tissue (Agency for Toxic Substances and Disease Registry 2012).

32. 1,4-Dioxane is a likely human carcinogen. EPA has classified 1,4-dioxane as "likely to be carcinogenic to humans" by all routes of exposure (Integrated Risk Information System 2013). The U.S. Department of Health and Human Services (DHHS) states that 1,4-dioxane is reasonably anticipated to be a human carcinogen based on sufficient evidence of carcinogenicity from studies in experimental animals (DHHS 2014). The National Institute for Occupational Safety and Health (NIOSH) considers 1,4-dioxane a potential occupational carcinogen (NIOSH 2010).

33. Short-term exposure to high levels of 1,4-dioxane may result in nausea, drowsiness, headache, and irritation of the eyes, nose and throat (Agency for Toxic Substances and Disease Registry 2012; Integrated Risk Information System 2013; NIOSH 2010; ECJRC 2002). An important feature of the scientific studies is a finding of consistent positive results in more than one type of animal model, which increases confidence in the results. Four inhalation studies in animals were identified in the literature; two, 13-week subchronic studies in laboratory animals (Kasai et al. 2009; Fairley, A; Linton, EC; Ford-Moore 1934) and two, 2-year chronic studies in rats (Kasai et al. 2009; Torkelson et al. 1974). Nasal, liver,

and kidney toxicity were the primary noncancer health effects of inhalation exposure to 1,4-dioxane in rodents.

34. 1,4-Dioxane is weakly genotoxic and its reproductive effects in humans are unknown; however, a developmental study on rats indicated that 1,4-dioxane may be slightly toxic to the developing fetus (Agency for Toxic Substances and Disease Registry 2012; Giavini, Vismara, and Broccia 1985). Studies in animal models have also reported that relatively high doses of 1,4-dioxane (1,000 mg/kg-day) during gestation can produce reduced fetal birth weights, which is an important marker for future health (Giavini, Vismara, and Broccia 1985).

35. Chronic studies reported the most sensitive effects in the liver and kidney in male Sherman rats from a high quality 2-year drinking water study (Kociba et al. 1974).

36. Long-term exposure to 1,4-dioxane may cause kidney and liver damage. (Agency for Toxic Substances and Disease Registry 2012; Integrated Risk Information System 2013; ECJRC 2002).

37. Due to concerns about the demonstrated serious health effects of 1,4-dioxane, 18 state health-based drinking water guidance values and federal occupational exposure limits have been established. EPA's IRIS database includes a chronic oral reference dose (RfD) of 0.03 milligrams per kilogram per day

(mg/kg/day) based on liver and kidney toxicity in animals, and a chronic inhalation reference concentration (RfC) of 0.03 milligrams per cubic meter (mg/m^3). (Integrated Risk Information System 2013). A chronic oral reference dose is a risk assessment benchmark or estimate of a daily oral dose to the human population (including accounting for sensitive subgroups and uncertainty) that is likely to be without an appreciable risk of deleterious non-cancer effects during a long-term period. A reference concentration is a similar risk assessment benchmark, referring to inhalation exposures.

38. Thus, people are exposed to 1,4-dioxane through multiple pathways including contaminated water, food, personal care products, and occupational exposures. The evaluation of the risks posed by these exposures must take into account the totality of those aggregate exposures in order to follow appropriate scientific procedures (National Academies of Sciences 2017; National Research Council 2009). Assessment of cumulative environmental exposures (e.g., to other chemicals) would also be recommended.

Conclusion

39. In my scientific opinion, 1,4-dioxane exposure may result in serious and in some cases permanent adverse health consequences for humans. These health effects are a cause for concern for current levels of 1,4-dioxane exposures. People are currently exposed via oral ingestion, inhalation and (to a lesser amount)

dermal contact pathways. Importantly, the risks posed by 1,4-dioxane are identical whether it is present by design or as a byproduct or contaminant. To fully assess the risks from 1,4-dioxane, a full consideration of the aggregate exposures must be undertaken.

Dated: April 13, 2018

Patricia Koman, Ph.D., MPP

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Exhibit A

to the Declaration of Patricia D. Koman, Ph.D., M.P.P.,
in Support of Petitioners' Opening Brief

Patricia D. Koman

524 3rd Street
Ann Arbor, MI 48103

tkoman@umich.edu
734-474-4711

Education

Doctor of Philosophy August 2016	University of Michigan, School of Public Health, Ann Arbor Environmental Health Sciences
Master of Public Policy May 1994	Graduate School of Public Policy, University of California, Berkeley
B.A. with Distinction May 1988	University of Virginia, Chemistry and Philosophy, *Phi Beta Kappa*; Louis Hammond Prize; Raven Society; Echols Scholar; Alpha Epsilon Delta science honorary society

Professional Experience

University of Michigan, School of Public Health, Ann Arbor, MI

(September 1, 2012 – present)

Research Investigator, Environmental Health Sciences (October 1, 2016 – present)
Interim Managing Director, Risk Science Center (September 1, 2016 – August 30, 2017)
Senior Project Manager, Dean's Office and Environmental Health Sciences Department (September 1, 2012 – August 31, 2016)

- Trained, mentored and developed scientists, faculty, and community members nationwide to communicate scientific data including evaluating epidemiologic studies with a variety of designs in regulatory decisions; team recommendations to Agency executives have been accepted, resulting in new research priorities, discussion in *Federal Register* records of decisions of additional data, and new and deeper involvement of medical sector stakeholders in environmental issues
- Initiated and led first School of Public Health (SPH) multi-disciplinary community-engaged project with Michigan Engaging Community Through the Classroom (MECC); co-investigator on three grants including 5-year $938,000 UM Third Century Transformative Learning grant for interdisciplinary engaged learning
- Conducted longitudinal secondary analysis of cohort data to examine the association between air pollution exposures with pulmonary function; performed an exposure assessment to assign air quality measurements to individual participants based on residential history and exam date; examined effect modification by obesity status of the relationship between air pollution exposure and lung function
- Principal investigator for MI-Environment cumulative environmental exposure vulnerability mapping and wildfire and health grants
- Developed environmental education curriculum and evaluation; as part of community-participatory process assisted with training of over 900 Flint residents about water quality and the drinking water system
- Led statewide training needs assessment of environmental health professionals to prepare public health workforce and target Michigan Public Health Training Center national course offerings, resulting in improved customer service competencies and skill in communicating complex issues to decision makers
- Provided expert consultation and testimony

- Michigan Department of Environmental Quality (MDEQ) Expert Panel to review water quality data from the city of Flint and recommendations with Michigan Governor Snyder's Flint Water Interagency Coordinating Council (FWICC) (2016- present)
- SPH Dean's Practice Advisory Committee (2012-2016)
- MDEQ technical advisory group for hazardous chemical clean-up standards (2013-14)

U.S. Environmental Protection Agency (June 1991 – August 30, 2012)

Environmental Scientist, Program Manager and Supervisor

- Office of Transportation and Air Quality, Ann Arbor, MI (2001 – August 30, 2012)
- Office of Air Quality Planning and Standards, Durham, NC (1994 – 2001)
- Region 9 Office, San Francisco, CA (June 1991 – 1994)

- Program Manager for Clean Ports USA: Achieved significant public health benefits by leading teams to reduce diesel emissions at U.S. seaports; in 5 years grew initiative to $100 million EPA grant program with projects on every coast and significant private investment
  - Developed Agency-wide multi-media marine ports strategy and budget request with EPA Administrator and Regional Administrators; communicated complex risk and exposure information to executives
  - Improved performance of 15-person cross-Agency multi-disciplinary team by creating new vision, managed operations and marketing campaign including web and print; supported 20 press announcements by top EPA executives and U.S. Senators; improved procedures for $125,000 public and technical information line to better communicate meaningful data to public
  - Forged key relationships with maritime industry, state and local agencies and other federal partners; developed regional networks by hosting technology conferences across the country; supported Agency executives' development of strategic plan in U.S., Taiwan, Panama and China
  - Initiated $2 million 6-party international partnership to develop prototype hydraulic hybrid yard hostler featuring EPA-patented technologies; displayed vehicle at international meetings by EPA Administrator; prototype tested in commercial service achieving emissions and fuel savings
  - Brought group to consensus over significant barriers as co-chair of Federal advisory workgroup under Mobile Source Technical Review Subcommittee
- Team leader of Implementation Strategies team responsible for budget formulation, communications and project implementation of the National Clean Diesel Campaign, developed web site with 80,000 hits and 40,000 copies of brochures describing health impacts of programs in the hands of clients each year; Charter developer of Clean School Bus USA nationwide public-private $150 million partnership measurably improving children's health

- Principal author of first Diesel Emissions Reduction Program Report to Congress; interpreting new legislative mandates; managed operations and improved software and web platform development of database to track, evaluate, and publicize projects; developed team with junior staff through coaching

- Program manager for multi-disciplinary scientific team conducting benefit-cost assessments of health and environmental improvements from major federal mobile source policies; authored air quality and public health justification for major rulemakings that withstood court challenges; worked with scientific advisory boards
  - Convened and led multi-disciplinary teams with annual budgets in excess of $500,000 to deliver complex modeling tasks on-time and under budget for Clean Air Act regulation of diesel emissions from heavy duty vehicles, nonroad equipment, and marine vessels while improving assessment methods and guiding research

- Principal author and team leader of landmark national air pollution standards for fine particulate matter under court ordered schedule; led 20-person multi-disciplinary scientific team and managed $1 million budget; analysis served as basis for policy that survived challenge to U.S. Supreme Court and became a top national priority for the EPA over the ensuing decade; required extensive evaluation of epidemiologic and air quality data

- As Air Toxics Center Director, supervised 11 engineers and specialists; managed all aspects of major Clean Air Act rulemaking; formulated and managed center's annual budget and resource request for 5-year plan

- As Coatings and Consumer Products Group Manager, supervised 12 engineers and Ph.D. scientists; responsible for personnel actions, health & safety and security policies for employees; managed all aspects of regulatory development and technical support for 28 new Clean Air Act actions; managed $2.3 million budget; advised senior management and prepared EPA witnesses for Congressional hearings; represented office to key stakeholders; briefed Congressional staff and the Office of Management and Budget staff; managed response to comment on six volume Report to Congress; interpreted legislation for first national rulemaking

SRI International, Research Analyst, Menlo Park, CA (1990 – 1991)
Conducted competitive assessments to create corporate strategies regarding environmental issues

ICF Incorporated, Analyst, Washington, DC (1988 – 1990)
Analyzed economic and technical impacts of broad array of environmental programs

Professional Honors and Awards

2017 National Center for Atmospheric Research Weather, Climate and Health Workshop Travel Scholarship
2017 University of Michigan "Road Scholar" Participant
2016 American Public Health Association Leadership Challenge Winner
2016 University of Michigan Graham Institute Dow Distinguished Interdisciplinary Sustainability Award
See for Yourself: What's in Your Water? Model Building
2015 University of Michigan Provost Teaching Innovation Prize
Michigan Engaging Community Through the Classroom (MECC)
2015 University of Michigan Graham Institute Dow Distinguished Interdisciplinary Sustainability Award
MI-Environment: Heat Stress Vulnerability Mapping
2014 University of Michigan, School of Public Health, Risk Science Fellowship
2014 University of Michigan Graham Institute Dow Distinguished Interdisciplinary Sustainability Award
MECC, Willow Run
2013 U.S. Health Resources and Services Administration and Association of Schools and Programs of Public Health "Promising Practice" recognition for MECC collaborative project teaching innovation
2012 Toastmasters International, Advanced Leadership – Silver
2011 Toastmasters International, Advanced Communication - Silver
2006 U.S. Environmental Protection Agency (EPA) Administrator's Award for Excellence
Economic Benefit Assessment Method Development
2007 U.S. EPA Gold Medal for Exceptional Service, Clean Diesel Initiative Team
2005 U.S. EPA Gold Medal for Exceptional Service, Clean Air Nonroad Diesel Rule Team
2004 U.S. EPA Silver Medal for Superior Service. Economic Benefits Methods Development
2003 U.S. EPA Bronze Medal for Commendable Service
2002 U.S. EPA Gold Medal for Exceptional Service, Heavy Duty Diesel Engine and Fuel Rule Team
2002 U.S. EPA Bronze Medal for Commendable Service
2001 U.S. EPA Role Model Award
1999 U.S. EPA Bronze Medal for Commendable Service
1998 U.S. EPA Gold Medal for Exceptional Service, Particulate Matter National Ambient Air Quality Standards
1997 U.S. EPA Bronze Medal for Commendable Service, Particulate Matter National Ambient Air Quality Standards Staff Paper

Grants

ACTIVE

1. University of Michigan Graham Institute Catalyst Grant. Atmospheric Modeling in Human Health & Climate Change Risk Assessment: Wildfire Smoke Exposures, $10,000 Principal Investigator (2017)

2. U.S. Environmental Protection Agency Environmental Education Grant, See for Yourself: What's in Your Water? Flint, Michigan $122,333, program manager and grant writer (2016-2017, PI Dvonch)

3. NIH/NIEHS Michigan Life Stages Environmental Exposures & Disease, NIEHS Center grant P30ES017885, University of Michigan, Co-Investigator, Integrated Health Sciences Core (2016, 5-year grant, PI Loch-Caruso)

4. University of Michigan, Third Century Transformative Learning Grant, Michigan Engaging Community Through the Classroom, $938,000 Co-Investigator (2015, 5-year grant, PI Norton)

COMPLETED

1. NIH/NIEHS Michigan Life Stages Environmental Exposures & Disease, NIEHS Center grant P30ES017885, University of Michigan, Pilot Grant: Climate and cardiopulmonary health: Does excess weight enhance risk? $5,600, Principal Investigator (2017)

2. NIH/NIEHS P30 ES017885 Community Outreach and Engagement Core (COEC) Supplement, 16-PAF08052, Environmental Justice Academy $100,000, Co-Investigator (2016, PI Schulz)

3. NIH/NIEHS Pilot grant, Michigan Life Stages Environmental Exposures & Disease P30ES017885, MI-Environment: Promoting Climate-Related Health within Michigan's Vulnerable Communities, $9,342 Co-Investigator (2016, PI Sampson)

4. University of Michigan, Graham Institute, Distinguished Interdisciplinary Sustainability Award, See for Yourself: What's in Your Water model development pilot, $5,000 Co-Investigator (2016, PI Olson)

5. University of Michigan President Fund, See for Yourself: What's In Your Water? Model Building, $3,600 Co-Investigator (2016, PI Daigger)

6. University of Michigan, Arts of Citizenship Award, MI-Environment: Hazard Proximity in Kent County, Michigan, $8,500 Principal Investigator (2015)

7. University of Michigan, Rackham Graduate Doctoral Candidate Award, $3,000 Principal Investigator (2015)

8. University of Michigan, Graham Institute, Distinguished Interdisciplinary Sustainability Award, MI-Environment: Climate Change and Heat Stress Vulnerability, $5,000 Co-Investigator (2015 PI O'Neill)

9. University of Michigan, Graham Institute, Distinguished Interdisciplinary Sustainability Award, Michigan Engaging Community Through the Classroom: Willow Run, $8,000 Co-Investigator (2014, PI Kellbaugh)

10. Michigan Public Health Training Center, Pilot Collaborative Project, Michigan Engaging Community Through the Classroom, $8,500 Principal Investigator (2013)

11. Rackham Graduate Student Award, University of Michigan, $1,500 Principal Investigator (2013)

Peer-Reviewed Publications

Koman PD, Mancuso P. 2017. Ozone exposure, cardiopulmonary health, and obesity: a substantive review. Chem. Res. Toxicol. acs.chemrestox.7b00077; doi:10.1021/acs.chemrestox.7b00077. ISSN 0893-228X. PMID 28574698 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5556919

Koman, P.D. K. Hogan, R. Mandell, N. Sampson, C.M. Coombe, Y. Hill-Ashford, M.M. Tetteh, D. Wilkins, R. Loch-Caruso, A. J. Schulz, T Woodruff. Air Pollution Exposure and Susceptibility of Pregnant Women: Disparities in Public Health Protection under the Clean Air Act (*Revision under review*)

Koman, P.D., J. Lam, T.J. Woodruff. The Promise and Perils of the Lautenberg Chemical Safety Act. (*Invited commentary manuscript, preparing resubmission)*

Norton, R.K., N.P. David, S. Buckman, **P.D. Koman**, Land Use Planning for Climate Change Adaptation on the Laurentian Great Lakes (*Revision under review*)

R.K. Norton, R. K., P. Fontaine, E.R. Gerber, G. Hohner, **P.D. Koman.** Pulling Aside Professional Blinders to Better Tackle Wicked Problems Through Multidisciplinary Community-Service Learning (*Revision under review*)

Manuscripts in Preparation

Koman, P.D., S.K. Park, C. Gronlund, D.J. Jacobs, Jr., P. Gordon-Larsen, P. Mancuso, M. O'Neill, Long-term Particulate Matter and Ozone Exposure and Pulmonary Function: Does Excess Weight Increase Risk? (Approved via CARDIA publication committee for submission, *manuscript in preparation*)

Koman, P.D., F. Romo, C. Gray, N. Sampson, S. Landfried, M. Battaglia, R Goodspeed, M.S. O'Neill, A.J. Schulz. MI-Environment: Heat Stress Vulnerability in Michigan Communities (*Manuscript in preparation)*

French, NH, M Billmire, JT Dvonch, S Hoshiko, J Hutchninson, **P.D. Koman**, MS O'Neill, CE Reid, A Steiner, BJ Thelen, S Wu. Modeling Wildland Fire Smoke Exposure for Quantifying Human Health Associations (*First draft prepared)* (after first author, authors listed alphabetically)

Peer Reviewed Reports

1. "Report to Congress: Highlights of the Diesel Emissions Reduction Program, Energy Policy Act of 2005," US EPA Office of Air and Radiation report, EPA-420-R-09-006, August 2009 (Principal author)

2. "Study and Report to Congress on Section 183(e), Response to Comments" U.S. EPA, Office of Air and Radiation report, EPA-453/R-98-007, August 1998 (Managing director)

   The Section 183(e) Study is composed of six volumes:
   (1) Report to Congress (EPA–453/R–94–066–a)
   (2) Comprehensive Emissions Inventory (EPA–453/R–94–066–b)
   (3) Fate of Consumer Product VOC in Landfills (EPA–453/R–94–066–c)
   (4) Fate of Consumer Product VOC in Wastewater (EPA–453/R–94–066–d)
   (5) Economic Incentives to Reduce VOC Emissions from Consumer and Commercial Products (EPA–453/R–94–066–e)
   (6) Aerosol Products and Packaging Systems (EPA–453/R–94–066–f)

3. "Review of the National Ambient Air Quality Standards for Particulate Matter: Policy Assessment of Scientific and Technical Information," U.S. EPA Office of Air and Radiation report, EPA-452\R-96-013, July 1996 (Principal author)

Government Reports with Peer Reviewed Methodologies

1. "MOVES Operating Mode Distribution Generator," U.S. EPA Office of Transportation and Air Quality, EPA-420-B-12-037, May 2012

2. "The National Clean Diesel Campaign (NCDC) 2005 Progress Report," U.S. EPA Office of Transportation and Air Quality, EPA-420-R-06-009, June 2006

3. "Regulatory Impact Analysis: Nonroad Diesel Engines and Fuel," (Chapter 2: Air Quality, Health and Welfare, and Chapter 9: Benefit-Cost Analysis), U.S. EPA Office of Air and Radiation report, May 2004

4. "Final Regulatory Support Document: Control of Emissions from New Marine Compression-Ignition Engines at or Above 30 Liters per Cylinder"(Chapter 2: Air Quality, Health and Welfare and Chapter 3: Industry Characterization) U.S. EPA Office of Air and Radiation report, EPA420-R-03-004, January 2003

5. "Regulatory Impact Analysis: Large SI/Recreational Vehicles Control," (Chapter 2: Air Quality, and Chapter 9: Benefit-Cost Analysis), U.S. EPA Office of Air and Radiation report, September 2002

6. "Regulatory Impact Analysis: Heavy-Duty Engine and Vehicle Standards and Highway Diesel Fuel Sulfur Control Requirements," (Chapter VII: Benefit-Cost Analysis), U.S. EPA Office of Air and Radiation report, EPA420-R-00-026, December 2000

7. "2018 Milestone Benefits Assessment of BART Reductions in 9 Western States," U.S. EPA Office of Air Quality Planning and Standards report, http://www.epa.gov/ttn/ecas/regdata/Benefits/milestone.pdf August 2000

Translational Publications and Technology Demonstrations

1. **Koman, P.D.**, P. Goldberg, C. Klawuhn, M. Swain, P.D. Meadows, "Environmental Health Professionals Training Needs Assessment," University of Michigan, Office of Public Health Practice report, Ann Arbor, MI, 2014

2. Anthony, M., **Koman, P.D.**, Storton M. Revisiting the Campus Power Dilemma: A Case Study. Planning for Higher Education Journal. Vol 4. No. 1, http://www.scup.org/phe. December 2013

3. "Clean Ports USA: Navigating Toward Cleaner Air," US EPA, Office of Transportation and Air Quality, EPA-420-F-10-023, 2010

4. Federal Laboratory Consortium for Technology Transfer calendar, Hydraulic hybrid yard hostler featured as EPA's technology of the year, 2010 (Project initiator, work assignment manager, team leader for $2 million 6-party international partnership)

5. Prototype hydraulic hybrid yard hostler displays featuring EPA-patented technologies:
- US EPA Administrator press event, Port of New York and New Jersey, 2008
- Society of Automotive Engineers World Congress, Detroit, April 2009
- World Maritime Day Parallel event "Climate Change: A Challenge for IMO too! Responding to a Changing Environment" October 2009

6. "National Clean Diesel Campaign: Working Together for Cleaner Air," US EPA, Office of Transportation and Air Quality, EPA-420-F-09-063, 2009

7. "National Clean Diesel Campaign: State and Local Government Tools and Resources," U.S. EPA, Office of Transportation and Air Quality, EPA-420-F-09-070, 2009

8. "National Clean Diesel Campaign: Funding your Clean Diesel Project, " U.S. EPA, Office of Transportation and Air Quality, EPA-420-F-09-071, 2009

9. "Health Benefits Due to Emission Reductions Attributed to National Clean Diesel Campaign Scenarios," with Abt Associates, September 2007

10. **Koman, P.D.**, and Blubaugh, J. "Ports and Politics: Ports Working Together to Achieve Cleaner Air," pp. 25-27, Seaports, Winter 2007
http://www.aapaports.org/Publications/SeaportsDetail.cfm?itemnumber=3518#seaportsarticle7

11. **Koman, P.D.** "Common Goals," Bunkerspot Journal, Vol. 4, No. 1, February 2007

12. **Koman, P.D.** "Clean Ports USA: Navigating to Cleaner Air," Bunkerspot Journal, April 2006

13. "Reducing Idling for Clean Air," U.S. EPA, Office of Transportation and Air Quality, EPA-420-H-06-001, April 2006

14. "25 Million Reasons Why It's Important to Reduce Idling," U.S. EPA, Office of Transportation and Air Quality, EPA-420-F-06-018, April 2006

15. "Reducing School Bus Idling: The Key to a Healthier Ride Training Video," U.S. EPA, Office of Transportation and Air Quality, EPA-420-V-04-001 and EPA-420-CD-04-001, August 2004

16. Small, M, **Koman, P.D.**, Rodrieguez, M, Savage, M.K., "State Money Talks: State Assurance Funds are Shaping Compliance and Corrective Action," Soils, pp. 24- 33. April 1993

17. Small, M., **Koman, P.D.**, Rodriguez, M, Savage, M.K. State Assurance Funds and their Impact on Underground Storage Tank Compliance and Remediation. Edward J Calabrese and Paul T Kostecki (Ed.), Hydrocarbon Contaminated Soil, Vol. 3 (pp. 653-752). Lewis Publishers, Chelsea, MI. ISBN 1-56670-018-3 1993.

Conference Leadership

1. University of Michigan, School of Public Health, Inaugural Environmental Health Practice Workshop, "Health Equity at Industrial Scale – Lautenberg Chemical Safety Act Under the Trump Administration," Ann Arbor, MI (steering committee chairperson, panel moderator, March 28, 2017)

2. University of Michigan, School of Public Health, Environmental Health Sciences, 75th Anniversary Celebration (steering committee chairperson, February 2017)

3. University of Michigan, School of Public Health, Nursing Grand Rounds, Healthy Built Environment: Nursing Strategies at the Policy, Program, and Patient Levels, Ann Arbor, MI (steering committee member) http://miphtcdev.web.itd.umich.edu/trainings/healthy-built-environments-nursing-strategies-policy-program-and-patient-levels-0 April 4, 2016

4. University of Michigan, School of Public Health, Public Health Leadership Summit, Blue Skies with Green Allies: A Role for All Sectors in Environmental Health, Ann Arbor, MI (steering committee member) http://miphtcdev.web.itd.umich.edu/trainings/blue-skies-green-allies-role-all-sectors-environmental-health September 16, 2015

5. Clean Diesel 10: National Clean Diesel Campaign Tenth Anniversary Celebration, Washington, DC (steering committee chairperson, technical conference chairperson, staffed EPA Assistant Administrator Gina McCarty and EPA Office Director) October 19-20, 2010

6. U.S. EPA Regional Administrators' Leadership Forum: Ports and Sustainability Strategic Planning, Baltimore, MD (steering committee chairperson, staffed EPA Office Director) July 14, 2010

7. 2009 World Maritime Day Co-Located Event, New York, NY (steering committee member, staffed U.S. EPA Assistant Administrator Gina McCarty, assisted with award to International Maritime Organization Secretary General and recognition of Consul General for the Netherlands) October 16-18, 2009

8. U.S. EPA Diesel Emissions Reduction Act Regional Collaborative Leadership meeting, San Diego, CA, (Steering committee member) February 2009

9. U.S. EPA Regional Administrator's Leadership Forum: Goods Movement and Marine Ports Strategic Planning, New York, NY (Steering committee member, staffed EPA Office Director) September 2008

10. U.S. EPA National Clean Diesel Campaign Regional Leadership Forum, Baltimore, MD (Steering committee member) 2007

11. Clean Ships: Advanced Technology for Clean Air, San Diego, CA (Steering committee chairperson, technical conference chairperson, staffed EPA Assistant Administrator) February 7-9, 2007

12. U.S. EPA Regional Administrator's Leadership Forum: Implications of Port Operations and Growth, Ports Strategic Planning Retreat, Long Beach, CA (Steering committee chairperson, staffed Deputy EPA Administrator Marcus Peacock and EPA Regional Administrator Steve Johnson) September 6 -7, 2006

13. Clean Ports USA Technology Workshops, Seattle, WA; Duluth, MN; New York, NY; Philadelphia, PA; Houston, TX, 2005-2006 (managing director)

14. U.S. EPA National Clean Diesel Campaign, Policy Leaders Summit, Baltimore, MD, (steering committee member), February 2005

15. Clean Ports USA Summit, Corpus Christi, TX (Steering committee chairperson, conference chairperson), January 2005

Posters and Conference Proceedings

1. Sutton, P., J. Lam, **P.D. Koman**, T.J. Woodruff. The perils and promise of TSCA for protecting children from exposure to toxic environmental chemicals. American Public Health Association, Atlanta, GA, October 2017 (*abstract accepted for oral presentation*)

2. **Koman, P.D**. N. Sampson, R. Mandell, C.M. Coombe, M.M. Tetteh, Y. Hill-Ashford, D. Wilkins, R. Loch-Caruso, A. J. Schulz, T Woodruff. Air Pollution Exposure and Susceptibility in Pregnant Women: Improving Public Health Protection under the Clean Air Act. American Public Health Association, Atlanta, GA, October 2017 (*abstract accepted for oral presentation*)

3. **Koman, P.D.**, S. Bailey, E. DeLoney, D Moses, K. Keys, S. Cupal, M. Munroe-Younis, T. Dvonch. "Community Participatory Principals in Water Quality Environmental Education Program in Flint, MI" Genesee County Health Department Conference, Flint, MI, May 9, 2017

4. French, N.H., K. Anthony, K. Baker, M. Billmire, S. Hoshiko, J. Hutchinson, J. Johnson, **P.D. Koman**, B. Koziol, V. Limaye, J. McCarty, R. C. Owen, C. Reid, B. Thelen, S. Wu. Approaches and challenges to connecting exposure to air pollution from wildland fire emissions to health outcomes. Planetary Health and GeoHealth Annual Meeting, Boston, MA, April 29, 2017

5. **Koman, P.D.**, F. Romo, C. Gray, N. Sampson, S. Landfried, M. Battaglia, K Hill-Knott, N.H. French, M.S. O'Neill, A.J. Schulz. MI-Environment Geospatial Analysis: Promoting Climate-Related Health within Michigan Vulnerable Communities. Planetary Health and GeoHealth Annual Meeting, Boston, MA, April 29, 2017

6. **Koman, P.D.**, F. Romo, C. Gray, N. Sampson, S. Landfried, M. Battaglia, M.S. O'Neill, A.J. Schulz. MI-Environment: Climate and Health in Michigan. National Institute for Environmental Health Sciences (NIEHS) 50th Anniversary Research conference, Durham, NC, December 8, 2016

7. **Koman, P.D.**, F. Romo, C. Gray, N. Sampson, S. Landfried, M. Battaglia, M.S. O'Neill, A.J. Schulz. MI-Environment: Promoting Climate-Related Health within Michigan Vulnerable Communities. American Public Health Association, Denver, CO, October 31, 2016

8. **Koman, P.D**. K. Hogan, K. Ferguson, R. Mandell, N. Sampson, C.M. Coombe, Y. Hill-Ashford, M.M. Tetteh, D. Wilkins, R. Loch-Caruso, A. J. Schulz, T Woodruff. Air Pollution Exposure and Susceptibility of Pregnant Women: Gender Disparities in Public Health Protection under the Clean Air Act. Social Determinants of Health Conference. George

Mason University School of Policy, Government and International Affairs. Arlington, VA. September 15, 2016

9. **Koman, P.D.** and P. Mancuso. Ozone exposure, obesity and occupational health. University of Michigan, School of Public Health, Center for Occupational Health & Safety Engineering symposium, Ann Arbor, MI, March 18, 2016

10. **Koman, P.D.** and P. Mancuso. Ozone exposure, obesity and cardiopulmonary health. University of Michigan, School of Public Health, Environmental Health Sciences Department Symposium, Ann Arbor, MI, January 22, 2016

11. **Koman, P.D.**, R. Adhikari, S.D. Adar, B.S. Kweon, P. Mohai, "Michigan School Children Proximity to Leaking Underground Storage Tanks and Hazardous Waste Treatment, Storage and Disposal Sites," American Public Health Association, Chicago, IL, November 4, 2015

12. Norton, R.K., P. Fontaine, E. Gerber, G. Hohner, **P.D. Koman**, J. Kosteva. "Generating Multidisciplinary Synergies across Community-Engaged Courses," University of Michigan, Center for Learning and Teaching Research conference, http://www.crlt.umich.edu/tip_winners, Ann Arbor, MI, May 5, 2015

13. **Koman, P.D.**, R. Adhikari, S.D. Adar, B.S. Kweon, P. Mohai, "Michigan School Children Proximity to Leaking Underground Storage Tanks and Hazardous Waste Treatment, Storage and Disposal Sites," University of Michigan, Environmental Health Sciences Department Symposium, Third Place poster award, Ann Arbor, MI, January 23, 2015

14. **Koman, P.D.,** P. Goldberg, C. Klawuhn, M. Swain, P.D. Meadows, "Environmental Health Professionals Training Needs Assessment," University of Michigan, Environmental Health Sciences Department Symposium, Ann Arbor, MI, January 23, 2015

15. Hill-Ashford, Y., **P.D. Koman**, K. Hogan, R. Mandell, A.J. Schulz, M. Tetteh, D. Wilkins, "Engaging community and academic partners in efforts to refine definitions of vulnerable populations: Detroit Reproductive Environmental Advocacy Matters (DREAM) Team," American Public Health Association conference, 299816, New Orleans, LA, November 17, 2014

16. Adar, S.D., M.S. Daskin, S.R. Gosman, **P.D. Koman**, B.S. Kweon, P. Mohai, "School Siting: Are Michigan Schools Safeguarding Children's Environmental Health," University of Michigan, MCubed Symposium, Ann Arbor, MI, October, 2014 (authors listed alphabetically)

17. Hogan K.A., M. Tetteh, R. Mandell, Y. Hill-Ashford, D. Wilkins, L. Nguyen, **P.D. Koman**, A.J. Schulz, C. Thomasson, S. Dernek, J. Jones, D. Ogunyemi, R. Loch-Caruso, "The DREAM Team and Clinical Allies Go to Washington: Environmental Reproductive Advocacy in Action," Michigan Community Health and Research Conference, Ann Arbor, MI, October 1, 2014

18. Thorpe, K., D. Thoe, **P.D. Koman**, "Michigan Engaging Community Through the Classroom: Willow Run Sustainability Project," University of Michigan, Undergraduate Research Opportunity Program (UROP) Symposium, Blue ribbon winner, Ann Arbor, MI, August 2014

19. Burke, M.N., **P.D. Koman**, P. Goldberg, C. Klawuhn, M. Swain, P.D. Meadows, "Environmental Health Professionals' Training Needs Assessment," University of Michigan, Undergraduate Research Opportunity Program (UROP) Symposium, Ann Arbor, MI, April 2014

20. Adar, S.D., M.S. Daskin, S.R. Gosman, **P.D. Koman**, B.S. Kweon, P. Mohai , "School Siting: Are Michigan Schools Safeguarding Children's Environmental Health," University of Michigan, MCubed Symposium, Ann Arbor, MI, November 15, 2013 (authors listed alphabetically)

21. **Koman, P.D.**, M. Arquero De Alarcon, P. Fontaine, C. Wilson, A. Yee, P. Barclay, M. Duchemin, N. Hall, A. Hing, Y. Mazloomdoost, E. Yu, D. Smith, P. Goldberg, D. Smith, D. Hawkins, P. Meadows, "Michigan Engaging Community

Through The Classroom. Collaborative community health impact assessment in the industrial landscapes of the Rust Belt: The Willow Run Project," Michigan Community Health and Research Conference, Ann Arbor, MI, March 19, 2013

22. Yee, A.K., **P.D. Koman**, M. Arquero de Alarcon, P. Barclay, M. Duchemin, P. Fontaine, P. Goldberg, N. Hall, A. Hing, Y. Mazloomdoost, E. Yu, D. Smith, D. Hawkins, C. Wilson, P. Meadows, "Michigan Engaging Community Through The Classroom. Community health and quality of life in the living industrial landscapes of the Rust Belt: The Willow Run Project," Poster and presentation at University of Michigan Rackham Graduate School Students of Color Conference, Ann Arbor, MI, March 22- 23, 2013

23. **Koman, P.D.**, C. Wilson, A. Yee, P. Barclay, M. Duchemin, N. Hall, A. Hing, Y. Mazloomdoost, E. Yu, D. Smith, P. Goldberg, P. Meadows, "Michigan Engaging Community Through The Classroom. Preliminary Health Impact Assessment." Poster and presentation at University of Michigan MECC final conference for project stakeholders, April 25, 2013; featured in AnnArbor.com news article

24. **Koman, P.D.**, Newstead, S., Keller, J., "Clean School Bus USA: Tomorrow's Buses for Today's Children," US EPA 3rd Annual Science Forum, Washington, DC June 2004

25. **Koman, P.D.**, Keller, J., Hubbell, B.J., "Reducing School Bus emissions: Successful solutions and practical applications," American Public Health Association 132rd Annual Meeting 5026.0 Disparities in Vulnerable Populations, Washington, DC, November 6-10, 2004

26. Hubbell, B., **P.D. Koman**, T. Fox, D. McCubbin, K. Davidson, P Dolwick. Health benefits of reducing particulate air pollution from nonroad diesel engines. Epidemiology. 15(4):S137. July 2004. ISSN: 1044-3983. DOI:1097/00001648-200407000-00355.

27. Hubbell, B., **P.D. Koman**, T. Fox, N.J. Possiel, G. Stella, B. Timin. Health benefits of reducing air pollution from heavy duty diesel engines. http://www.epa.gov/ttn/ecas/workingpapers/hddben.pdf, Research Triangle Park, NC, 2001

28. Hubbell, B.J., **Koman, P.D.**, Laurence, J., Heninger, B., Petro, A., Mills, J. and Haynes, R. "Integrated Forestry Ozone Regulatory Modeling System," Future Directions in Air Quality Research, North Carolina State University, Research Triangle Park, NC, February 12, 2001

29. Rogers, C.F., J.C. Chow, J.G. Watson, C.A. Cahill, S. Diaz , **P.D. Koman** , S. Sleva, R. Tropp, "Mineral Dust Contributions to Fine Particle Mass," Air & Waste Management Association, pp.168-176. January 1998

30. Small, M., Eklund, P., **Koman, P.D.** "Streamlining and Prioritizing Leaking Underground Storage Tank Site Corrective Action Programs," Proceedings of Air and Waste Management Conference, Accelerating Underground Storage Tank Corrective Action, Vol. 31, pp. 38-49, San Antonio, TX, March 1993

Preparation for Teaching

1. Participant, Graduate teaching certificate coursework, University of Michigan, Rackham Graduate School, Center for Research on Teaching and Learning, under mentorship of Dr. Phyllis Meadows, Health Management and Policy

    - Writing and Grading Exams virtual workshop, June 2015
    - Preparing Future Faculty Seminar, Spring Term 2015
    - Advanced Strategies for Inclusive Teaching workshop, March 2015
    - Graduate Student Instructor Orientation, January 2014

2. Syllabus design workshop. University of Michigan, Rackham Graduate School, Arts of Citizenship. Fall term 2014

3. Graduate Student Instructor Spring Board to Teaching seminar. University of Michigan, School of Public Health. Ann Arbor, MI. Fall 2013

Teaching, Training and Instruction

1. Practitioner roundtable for Rackham's Institute for Social Change introduction to public scholarship, "Working for Social Justice Inside and Outside Academia," University of Michigan, Rackham Graduate School, Ann Arbor, MI August 22, 2017

2. Master Class instructor, "Transportation Affects Health," Movin'On Michelin World Summit on Sustainable Transportation, Montreal, Canada, June 14, 2017

3. Guest lecture for Future Public Health Leaders program, for 40 undergraduate Center for Disease Control and Prevention scholars. "Environmental Health Sciences." University of Michigan, School of Public Health, Ann Arbor, MI, May 25, 2017

4. Curriculum co-developer, "Environmental Justice Academy" community-based participatory research partnership. Winter Term 2017

5. Curriculum developer and trainer, "See for Yourself: What's in Your Water" water quality and drinking water delivery system training for 500 community members and K-12 students in Flint, MI. Fall 2016 and Winter Term 2017

6. Assistant course instructor, PH600, Cross-disciplinary approaches to public health challenges, 4 credits, University of Michigan, School of Public Health, Associate Dean Phyllis Meadows. Winter Term 2016

7. Guest lecture for Future Public Health Leaders program, for 40 undergraduate Center for Disease Control and Prevention scholars. "Health Impact Assessment." University of Michigan, School of Public Health, Ann Arbor, MI. Associate Dean Phyllis Meadows. June 2015

8. Guest lecture for webinar, University of California San Francisco, Obstetrics, Gynecology and Reproductive Sciences, Reach the Decision Maker Fellows, for 50 health professionals, "Strategies for Effective Communication with the U.S. Environmental Protection Agency," Dr. Tracey Woodruff. June 2015

9. Guest lecture for Future Public Health Leaders program, for 40 undergraduate Center for Disease Control and Prevention scholars. "Environmental Health Sciences." University of Michigan, School of Public Health, Ann Arbor, MI. Associate Dean Phyllis Meadows. June 2015

10. Koman, P.D. "Climate Change and Human Health," Keynote. University of Michigan School of Public Health and Michigan Association for Local Public Health Day, Ann Arbor, MI, March 9, 2015 Available as Michigan Public Health Training Center on-line training: http://miphtcdev.web.itd.umich.edu/trainings/climate-change-and-human-health

11. Guest lecture for Future Public Health Leaders program, for 50 undergraduate Center for Disease Control and Prevention scholars. "Fundamentals of Health Impact Assessment." University of Michigan, School of Public Health, Ann Arbor, MI. Associate Dean Phyllis Meadows. July 2014

12. Invited trainer, University of California San Francisco, Obstetrics, Gynecology and Reproductive Sciences, Reach the Decision Maker Fellows, for 25 health professionals nationwide, "Making Your Case in Environmental Policy," Reach the Decision Maker Program, Washington, DC, Dr. Tracey Woodruff. May 2014

13. Guest lecture for webinar, University of California San Francisco, Obstetrics, Gynecology and Reproductive Sciences, Reach the Decision Maker Fellows, for 50 health professionals, "Effective Communication with the Environmental Protection Agency," Dr. Tracey Woodruff. June 2014

14. Guest lecture for Future Public Health Leaders program, for 50 undergraduate Center for Disease Control and Prevention scholars. "Introduction to Environmental Health Sciences." University of Michigan, School of Public Health, Ann Arbor, MI. Associate Dean Phyllis Meadows. June 2014

15. Guest lecture for 25 urban planning masters students, "Building Healthy Communities: Children's Environmental Health and Hazardous Substance Clean Up Criteria in Michigan." University of Michigan, Urban Planning Department. Ann Arbor, MI. UP 502 Environmental Planning, Issues and Concepts. Assistant Professor Ana Paula Pimental Walker. Fall 2013

16. Guest lecture for Future Public Health Leaders program, for 50 undergraduate Center for Disease Control and Prevention scholars. "Introduction to Environmental Health Sciences." University of Michigan, School of Public Health, Ann Arbor, MI. Associate Dean Phyllis Meadows. June 2013

17. Guest lecture on air quality and marine ports for masters students. University of Michigan, School of Public Health, Environmental Health Sciences. Ann Arbor, MI. EHS 572/SNRE 514 Environmental Impact Assessment. Professor Stuart Batterman. Fall 2012

18. Guest lecture for graduate students, "Ship Air Emissions and Controls," University of Michigan, College of Engineering, Naval Architecture and Marine Engineering. Ann Arbor, MI. Professor Jing Sun. Winter 2007

19. Trainer and course developer, "EPA Mobile Source Emissions software MOVES2010b Pilot Training Course." International Emissions Inventory Conference. 8-hour training, Tampa, FL. August 13, 2012

20. Trainer, "MOVES 3-Day Training Course," EPA Mobile Source Emissions Modeling 3-day computer-based training, Lansing, MI. May 2012

21. Trainer, "Effectively Communicating Key Messages," EPA's National Clean Diesel Campaign Regional Office Partners meeting. Washington, DC. December 9, 2005

Selected Presentations

1. **Koman, P.D.**, French, N.H., M.S. O'Neill, J.T. Dvonch, C. Reid, S. Hoshiko, K. Baker, M. Billmire, B. Thelen, S. Wu, A. Steiner. Atmospheric Modeling in Human Health & Climate Change Risk Assessment: Wildfire Smoke Exposures. Graham Institute external advisory board annual meeting, Ann Arbor, MI, April 13, 2017

2. **Koman, P.D.**, F. Romo, C. Gray, N. Sampson, S. Landfried, M. Battaglia, M.S. O'Neill, A.J. Schulz. MI-Environment: Promoting Climate-Related Health within Michigan Vulnerable Communities. University of Michigan Environmental Epidemiology research seminar, Ann Arbor, MI, February 14, 2017

3. **Koman, P.D.**, F. Romo, C. Gray, N. Sampson, S. Landfried, M. Battaglia, R Goodspeed, M.S. O'Neill, A.J. Schulz. MI-Environment: Heat Stress Vulnerability in Michigan Communities. Michigan University-wide Sustainability & Environment, Ann Arbor, MI, February 9, 2017

4. **Koman, P.D.** "Health Equity at Industrial Scale: What Every Public Health Professional Needs to Know about the Lautenberg Chemical Safety Act," California Department of Health research seminar, Richmond, CA, January 30, 2017

5. **Koman, P.D.,** M. Munroe-Younis. "See for Yourself: What's in Your Water?" Flint Neighborhood Recovery Resource Meeting, Flint, MI, January 5, 2017

6. **Koman, P.D.,** A. Jakkaraju, M. Halso, K. Heidecorn, C. Xi, T.M. Olson. "See for Yourself: What's In Your Water? Environmental Education Model Building." Environmental Water Resources Engineering Program Symposium, Ann Arbor, MI, October 21, 2016

7. **Koman, P.D.**, F. Romo, C. Gray, N. Sampson, S. Landfried, M. Battaglia, M.S. O'Neill, A.J. Schulz. MI-Environment: Promoting Climate-Related Health within Michigan Vulnerable Communities. American Public Health Association, Denver, CO, October 31, 2016

8. **Koman, P.D.** "See for Yourself: What's in Your Water?" Genesee County Steering Prevention Reducing Obesity Utilizing Teamwork (SPROUT), Genesse County Health Department, November 14, 2016

9. Panelist, Future Public Health Leaders program for 40 undergraduate Center for Disease Control and Prevention scholars, "Public Health Careers," University of Michigan, School of Public Health, Ann Arbor, MI. PI Associate Dean Phyllis Meadows. July 18, 2016

10. Norton, R.K., P. Fontaine, E. Gerber, G. Hohner, **P.D. Koman**, J. Kosteva. "Michigan Engaging Community Through the Classroom," University of Michigan, Center for Learning and Teaching Research conference, May 16, 2016

11. **Koman, P.D.,** keynote presentation, "Climate Change and Human Health" Genesee County Health Department 10th Annual Public Health Conference, Flint, MI, May 3, 2016

12. **Koman, P.D.**, F. Romo, S. Landfried, M O'Neill. "MI-Environment: Heat Vulnerability Mapping Interactive Tool" Michigan Lifestage Environmental Exposure & Disease Center pilot, Science Cafe, Detroit, MI, March 24, 2016

13. **Koman, P.D.**, Detroiters Working for Environmental Justice – "Communicating Climate Change and Health" interactive icebreaker activity at Climate Action Plan meeting in Detroit, MI

14. **Koman, P.D.,** invited panelist, "Engaging Community Partners," University of Michigan, Rackham Graduate School Arts of Citizenship Program training, Ann Arbor, MI, November 13, 2015

15. **Koman, P.D.,** invited speaker, "Climate Change and MI-Environment Heat Vulnerability Index: Opportunities for Research and Partnerships," University of Michigan, NIEHS Community Outreach & Engagement Core, Michigan Lifestage Environmental Exposure & Disease Center, Faculty and partners mobile meeting, Detroit, MI, November 13, 2015

16. F. Romo, M. Battaglia, **Koman, P.D.**, S. Landfried, M O'Neill, R. Goodspeed. "MI-Environment: Hazard Proximity in Kent County," Michigan Technology Research Institute, Ann Arbor, MI, October 30, 2015

17. **Koman, P.D.,** invited panelist, "Innovative Research," University of Michigan, Rackham Graduate School Donors Celebration Dinner, Ann Arbor, MI, October 9, 2015

18. Gronlund, C, **Koman, P.D.**, Cameron, L., Bryan, D. "Climate Change in Michigan: Human Health, Resilience, and Equity," Michigan Association for Local Public Health Premier Conference, Thompsonville, MI, October 7, 2015

19. **Koman, P.D.**, K. Huber, F. Romo, S. Landfried, R. Goodspeed, M O'Neill. "MI-Environment: Heat Vulnerability Mapping" NIEHS Community Outreach & Engagement Core, Michigan Lifestage Environmental Exposure & Disease Center, Stakeholder Advisory Board Meeting, Detroit, MI, July 22, 2015.

20. **Koman, P.D.,** national webinar, University of California San Francisco, Obstetrics, Gynecology and Reproductive Sciences, Reach the Decision Maker Fellows, for 50 health professionals, "Strategies for Effective Communication with the U.S. Environmental Protection Agency," June 2015

21. **Koman, P.D.**, P. Goldberg, C. Klawuhn, M. Swain, P.D. Meadows, "Michigan Environmental Health Professionals' Training Needs," Michigan Environmental Health Association conference, Traverse City, MI, March 20, 2015

22. **Koman, P.D.**, P. Goldberg, C. Klawuhn, M. Swain, P.D. Meadows, "The Future of Michigan Public Health Professionals: Strategic Directions and Training Needs," Michigan's Premier Public Health Conference, Michigan Association for Local Public Health, Bellaire, MI, October 22, 2014

23. **Koman P.D.**, "Risk Miscues and Mixed Messages: What is a Transportation Planner to Do?" 93rd Annual Transportation Research Board Conference, Washington, DC, January 12, 2014

24. **Koman, P.D**. and P. Mancuso, "Implications of Obesity Trends for Designating At-risk Populations in the Ozone and Particulate Matter National Ambient Air Quality Standards," American Public Health Association, 141st Annual Meeting, Boston, MA, November 4, 2013

25. **Koman, P.D.** "Understanding Michigan's Remediation and Redevelopment Program: What Every Public Health Official Needs to Know," Michigan's Premier Public Health Conference, Michigan Association for Local Public Health, Bay City, MI, October 17, 2013

26. **Koman, P.D.**, speaker and panel moderator, "Nonroad Engine Emissions Modeling," International Emissions Inventory Conference, Tampa, FL, August 16, 2012

27. **Koman, P.D.**, "Diesel Emissions Reduction Act Funding and Reauthorization," American Association of Port Authorities, Harbors, Navigation and Environment Committee Webinar, Charleston, SC, September 1, 2010

28. **Koman, P.D.**, "Diesel Emissions Reduction Act Reauthorization," Greenports and American Association of Port Authorities, Harbors, Navigation and Environment Committee Seminar, May 4-6, 2010

29. **Koman, P.D.**, keynote panel, "Future of the National Clean Diesel Campaign," Southeast Diesel Collaborative Annual Partners Meeting, Atlanta, GA, June 2009

30. **Koman, P.D.**, "Clean Ports USA," EPA Diesel Emissions Reduction Act Regional Collaborative Leadership meeting, San Diego, CA, February 2009

31. **Koman, P.D.**, "Sustainable Future - Hydraulic Hybrid Yard Hostler," U.S. – Taiwan Bilateral Environmental Cooperation meetings, and Taipei, Taiwan November 2008

32. **Koman, P.D.**, "Lessons from New York - Hydraulic Hybrid Yard Hostler," Pacific Ports Air Quality Conference, Kaohsiung, Taiwan, November 2008

33. **Koman, P.D.**, "U.S. Perspectives on Reducing Air Pollution from Ocean-Going Vessels," American Association of Port Authorities Conference, Panama City, Panama, May 2008

34. **Koman, P.D.**, "National Clean Diesel Campaign," Faster Freight - Cleaner Air, Los Angeles, CA, March 2008

35. **Koman, P.D.**, moderator and panel speaker, "Clean Ports USA: Reducing Emissions from Marine Engines," Faster Freight - Cleaner Air, Los Angeles, CA, March 2008

36. **Koman, P.D.**, "Communication and Outreach," EPA National Clean Diesel Campaign Regional Leadership Forum, Baltimore, MD, 2007

37. **Koman, P.D.**, "Clean Ports USA: Navigating to Cleaner Air," EPA National Clean Diesel Campaign Regional Leadership Forum, Baltimore, MD 2007

38. **Koman, P.D.**, "Clean Ports USA: Great Ideas for the Great Lakes," Great Lakes Ports Association Directors' Meeting, Cleveland, OH, June 2006

39. **Koman, P.D.**, "Clean Ports USA: Navigating toward Cleaner Air," State and Territorial Air Pollution Program Administrators (STAPPA) / Association of Local Air Pollution Control Officers (ALAPCO) annual meeting, Madison, WI, May 21-25, 2005

40. **Koman, P.D.**, "Clean Ports USA," National Association of Waterfront Employers' annual executives meeting, Charlotte, NC, April 2005

41. **Koman, P.D.**, "Clean Ports USA," Clean Ports USA Summit, Corpus Christi, TX, January 26, 2005

42. **Koman, P.D.**, "Clean School Bus USA Demonstration Projects," National Retrofit Conference, Washington, DC, June 2004

43. **Koman, P.D.**,"Clean School Bus USA," Maricopa Association of Governments, Phoenix, AZ, March 2004

44. **Koman, P.D.**, keynote speaker, "Moving the Air Toxics Program Forward," American Forest and Paper Association Conference, Research Triangle Park, NC, April 1999

45. **Koman, P.D.**, keynote speaker, "Pollution Prevention in EPA's Industrial Surface Coating National Emission Standards for Hazardous Air Pollutants," National Pollution Prevention Roundtable, Cincinnati, OH, May 1998

46. **Koman, P.D.**, "Ten Year Surface Coating National Emission Standards for Hazardous Air Pollutants," Air Toxics Implementation Workshop, Research Triangle Park, NC, August 1997

47. Trainer for nationally broadcast program (answering live questions from air pollution regulators, industry representatives, and other participants) regarding the final decision to revise the ozone and particulate matter (PM) national ambient air quality standards (NAAQS), July 1997

48. **Koman, P.D.**, keynote plenary address, "Proposed Revisions to the PM NAAQS," Air and Waste Management Association (AWMA) Utilities and Acid Rain Conference, Phoenix, AZ, January 1997

49. **Koman, P.D.**, plenary speaker, "Proposed Revisions to the PM NAAQS," American Forest and Paper Association Conference, Research Triangle Park, NC, February 1997

50. National spokesperson for proposed revisions to the PM NAAQS at Air and Waste Management Association public seminars, January and February 1997, at the following locations:

- Atlanta, GA	- New York, NY
- Chicago, IL	- Phoenix, AZ
- Hartford, CT	- Pittsburgh, PA
- Los Angeles, CA	- Research Triangle Park, NC

51. Presenter to Japanese and Russian delegation regarding the proposed revisions to the ozone and PM NAAQS, Research Triangle Park, NC, 1997

52. Lead presentation with in-depth 3-hour question-and-answer session at WESTAR meeting for Western State and local air pollution officials regarding proposed revisions to the PM NAAQS, Palm Springs, CA, December 1996

53. Trainer for seminar broadcast nationally (answering questions faxed in from air pollution regulators, industry representatives, and other participants) regarding proposed revisions to the Ozone and PM NAAQS, December 1996

54. Small, M., Eklund, P., **Koman, P.D.** "Streamlining and Prioritizing Leaking Underground Storage Tank Site Corrective Action Programs," US EPA National Underground Storage Tank Conference, Washington, DC, March 1993

Affiliations

- International Society for Environmental Epidemiology (2015- present)
- International Epidemiology Association (2016- present)
- American Public Health Association (2004, 2012- present)
- Michigan Engaging Community Through the Classroom Advisory Committee (2013- present)
- Mentor, Reach the Decision Makers program, University of California at San Francisco (2013 – 2016)
- Navigation Guide Group, University of California at San Francisco Program on Reproductive Health and the Environment (2012 – present)
- American Association of Port Authorities, Harbors Navigation and Environment Committee (associate member, 2005- 2011)

Exhibit 3

IN THE UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

SAFER CHEMICALS, HEALTHY FAMILIES et al., *Petitioners,* v. U.S. ENVIRONMENTAL PROTECTION AGENCY et al., *Respondents.* IPC INTERNATIONAL, INC. et al., *Respondents-Intervenors.*	Docket No. 17-72260 Consolidated with Docket Nos. 17-72501, 17-72968, 17-73290, 17-73383, 17-73390

DECLARATION OF DETLEF KNAPPE, PH.D., IN SUPPORT OF PETITIONERS' OPENING BRIEF

I, DETLEF KNAPPE, do hereby affirm and state:

Introduction and Qualifications

1. I am an environmental engineer. I hold a B.S. in Civil Engineering from the University of Illinois at Urbana-Champaign (1989). I received M.S. (1991) and Ph.D. (1996) degrees in Environmental Engineering from the University of Illinois at Urbana-Champaign.

2. I am a Professor in the Department of Civil, Construction, and Environmental Engineering at North Carolina State University in Raleigh. I teach two graduate courses (Chemical Principles of Environmental Engineering;

Physical-Chemical Water Treatment Processes) and one undergraduate course (Environmental Chemistry and Microbiology).

3. My research focuses on (1) developing and evaluating physical-chemical treatment processes for the control of trace organic contaminants (e.g., carcinogenic volatile organic contaminants, 1,4-dioxane, fluorochemicals, endocrine-disrupting chemicals, antibiotics, and other pharmaceutically active compounds), and (2) developing information about the effects of reactive and unregulated wastewater contaminants on drinking water quality and treatment—information that is not provided under the federal Clean Water Act or Safe Drinking Water Act.

4. I am a member of the Drinking Water Committee of the United States Environmental Protection Agency's Science Advisory Board. I am also a member of the Science Advisory Board of the North Carolina Department of Environmental Quality and the North Carolina Department of Health and Human Services

5. I serve as a Trustee for the Water Science and Research Division of the American Water Works Association, and am a member of the Association's Activated Carbon Standards Committee and the Organic Contaminants Research Committee.

6. A more complete description of my educational and work experience, as well as a complete list of my publications, is appended as Exhibit A.

7. By virtue of my engineering training, my research, my professional service, and knowledge of pertinent scientific literature, I consider myself—and others in the field consider me to be—an expert on trace organic contaminants and their effects on drinking water quality and treatment.

8. All of the information set forth in this declaration is based upon my education, personal knowledge, and experience.

What is 1,4-dioxane?

9. 1,4-Dioxane is an organic compound produced for commercial purposes. It is also a manufacturing by-product.

10. In the past, the dominant commercial use of 1,4-dioxane was for the stabilization of certain solvents. The use of 1,4-dioxane as a solvent stabilizer has decreased since 1995 when production of one such solvent was phased out under the Montreal Protocol (an international treaty) because of its ozone depletion potential.

11. Currently, 1,4-dioxane is used as a chemical reactant, solvent, and processing aid in many industries, such as textile processing, specialty chemical manufacturing (e.g., pharmaceuticals, pesticides), recycling, wood pulping,

manufacturing of polyethyleneterephthalate (PET) plastics, cellulose acetate, resins, waxes, and fats.[1]

12. 1,4-Dioxane can also be produced as a by-product in manufacturing processes, including production of polyester and surfactants used in detergents and shampoos.

13. 1,4-Dioxane is an impurity in some consumer products, including detergents, waxes, varnishes, and personal care products such as shampoos and cosmetics.

14. Reliable current 1,4-dioxane production volumes in the United States are not available because much of the information is considered confidential business information. Furthermore, there is no reliable information on the volume of by-products generated.

15. There is no federal drinking water standard for 1,4-dioxane.

16. Several states have developed drinking water standards or guidelines for 1,4-dioxane.

17. In North Carolina, a narrative surface water quality standard exists. 15A NCAC 02B .0208 states that "for carcinogens, the concentrations . . . shall not

[1] U.S. EPA, Rep. No. EPA-HQ-OPPT-2016-0723, Preliminary Information on Manufacturing, Processing, Distribution, Use, and Disposal: 1,4-Dioxane (2017), https://www.epa.gov/sites/production/files/2017-02/documents/14-dioxane.pdf.

result in unacceptable health risks and shall be based on a Carcinogenic Potency Factor. An unacceptable health risk for cancer shall be considered to be more than one case of cancer per one million people exposed (one-in-a-million risk level)." For 1,4-dioxane, the one-in-a-million risk level corresponds to a concentration of 0.35 μg/L (or parts per billion).

How widespread is 1,4-dioxane contamination of drinking water in the U.S.?

18. The U.S. Environmental Protection Agency (EPA) assessed the occurrence of 1,4-dioxane in U.S. drinking water as part of the Third Unregulated Contaminant Monitoring Rule (UCMR3).[2] Between January 1, 2013, and December 31, 2015, more than 36,000 drinking water samples were collected across the United States and submitted for 1,4-dioxane analysis. These samples came from almost 5,000 public water systems in the United States, each of which serves more than 10,000 people. Nationwide, 1,4-dioxane was detected in 21.9% of public water systems, and 1,4-dioxane levels exceeded 0.35 μg/L—the one-in-a-million risk level—in 6.9% of public water systems. More than 75% of all 1,4-dioxane detections in U.S. drinking water were associated with **groundwater** sources.

[2] *See* U.S. EPA, Occurrence Data for the Unregulated Contaminant Monitoring Rule, https://www.epa.gov/dwucmr/occurrence-data-unregulated-contaminant-monitoring-rule#3.

19. Compared to the entire United States, 1,4-dioxane occurs more frequently in North Carolina drinking water. Between January 1, 2013, and December 31, 2015, as part of the UCMR3, more than 1,300 drinking water samples were collected across North Carolina and submitted for 1,4-dioxane analysis. These samples came from 151 public water systems that serve more than 10,000 people. In North Carolina, 1,4-dioxane was detected in 30.5% of public water systems, and 1,4-dioxane levels exceeded 0.35 μg/L in 15.9% of public water systems. More than 95% of all 1,4-dioxane detections in North Carolina were associated with **surface water** sources.

How does 1,4-dioxane enter drinking water sources?

20. Most drinking water in the United States is produced from groundwater or surface water.

21. 1,4-Dioxane can enter groundwater from leaking underground storage tanks that contain(ed) solvents stabilized with 1,4-dioxane, from unlined landfills, and from wastewater lagoons.

22. 1,4-Dioxane can enter surface water through municipal and industrial wastewater treatment plant discharges.

23. The concentration of 1,4-dioxane in U.S. municipal wastewater discharges is typically found at levels that are associated with the use of consumer

products such as laundry detergents and shampoos. These levels generally range from 0.3 to 3 μg/L.[3]

24. In many communities, industrial wastewater is pre-treated and discharged to the municipal sewer. Because 1,4-dioxane is an unregulated contaminant, its possible presence is typically not considered when pre-treatment programs evaluate the discharge from an industrial wastewater treatment plant to a municipal sewer system.

25. If an industrial wastewater discharge to a municipal sewer contains high levels of 1,4-dioxane, it will elevate the 1,4-dioxane concentration of the wastewater reaching the municipal wastewater treatment plant. Municipal wastewater treatment plants cannot effectively remove 1,4-dioxane. Therefore, 1,4-dioxane concentrations will be high in the discharge of municipal wastewater treatment plants that receive industrial wastewater with elevated 1,4-dioxane concentrations.

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[3] Staci Massey Simonich et al., Probabilistic analysis of risks to US drinking water intakes from 1,4-dioxane in domestic wastewater treatment plant effluents, 9 Integ. Envtl. Assess. Mgmt. 554 (2013), https://setac.onlinelibrary.wiley.com /doi/epdf/10.1002/ieam.1448; Detlef R. U. Knappe et al., U. N.C. Water Res. Research Inst., Rep. No. 478, Occurrence of 1,4-Dioxane in the Cape Fear River Watershed and Effectiveness of Water Treatment Options for 1,4-Dioxane Control (2016), https://repository.lib.ncsu.edu/bitstream/handle/1840.20/34331/UNC-WRRI-478.pdf?sequence=1&isAllowed=y [hereafter Cape Fear Report].

26. In 2015, in North Carolina, the Department of Environmental Quality and North Carolina State University monitored 1,4-dioxane concentrations in the Cape Fear River watershed. Monthly samples were collected from October 2014 to October 2015 and analyzed. Discharges of three municipal wastewater treatment plants were found to be significant sources of 1,4-dioxane. The highest 1,4-dioxane concentrations (up to 1,700 μg/L) were observed in the headwaters of the Cape Fear River watershed just downstream of the three wastewater treatment plant discharges. Median 1,4-dioxane concentrations decreased in a downstream direction with increasing distance from the identified sources. However, the concentration of 1,4-dioxane stayed above the one-in-a-million risk level throughout the watershed.

How persistent is 1,4-dioxane in aquatic systems?

27. The molecular structure of 1,4-dioxane makes it stable and relatively immune to environmental degradation as it moves through a watershed.

28. Watershed monitoring data for the Cape Fear River basin in North Carolina are consistent with the persistent nature of 1,4-dioxane. Monthly monitoring in two rivers over a one-year period (October 2014-October 2015) demonstrated that mass flows of 1,4-dioxane remained stable over a 200-km-stretch of the Cape Fear River that had no substantial 1,4-dioxane inputs.[4] Similar

[4] Cape Fear Report.

results showing no losses of 1,4-dioxane were observed over a 120-km-stretch of the Deep River.

How can 1,4-dioxane be removed in drinking water treatment plants?

29. 1,4-Dioxane is not removed in conventional surface water treatment plants. Conventional surface water treatment processes include: (1) coagulation, (2) flocculation, (3) solid-liquid separation (e.g., sedimentation, filtration), and (4) disinfection with free chlorine. A 2014 North Carolina State University study of two drinking water treatment plants in the Cape Fear River watershed showed no removal of 1,4-dioxane.[5] For the Pittsboro plant, the finished drinking water contained 1,4-dioxane at levels 25 times the one-in-a-million risk level. For the Fayetteville plant, the finished drinking water contained 1,4-dioxane at levels 7 times the one-in-a-million risk level.

30. 1,4-Dioxane is also not well removed by many advanced treatment technologies, including activated carbon adsorption, air stripping, and most oxidation processes (including treatment by chlorine).

31. There are some advanced treatment options that can remove 1,4-dioxane from drinking water, such as ultraviolet light in combination with hydrogen peroxide or ozone. Data from our laboratory suggest that implementing

[5] *Id.*

such treatment required to lower 1,4-dioxane to safe levels in the Cape Fear River basin would be very costly.

32. Advanced treatment with ozone at a drinking water treatment plant in Wilmington, North Carolina was insufficient to lower the 1,4-dioxane concentration to the one-in-a-million risk level (0.35 μg/L). Ozone treatment may also create undesirable by-products in some water systems.

33. Reverse osmosis membranes may partially remove 1,4-dioxane, but may need to be coupled with other advanced treatment to achieve safe levels. Such treatment is very costly compared to conventional treatment.

How many North Carolinians drink water with elevated 1,4-dioxane levels?

34. Surface water in the Cape Fear River basin serves as a source of drinking water for approximately 1.5 million North Carolinians. Of the approximately 1.5 million residents, about 1 million receive drinking water with 1,4-dioxane concentrations above the one-in-a-million risk level.

What can affected residents do?

35. To date, no point-of-use (pitcher, faucet, under-sink, refrigerator) or point-of-entry (whole house) filters have been certified for 1,4-dioxane removal.

36. Pitcher and refrigerator filters were evaluated at North Carolina State University for their 1,4-dioxane removal effectiveness. Overall, commercially available point-of-use treatment devices exhibited limited effectiveness for 1,4-

dioxane removal from tap water, especially under variable 1,4-dioxane concentrations.[6]

37. In a field study involving six under-sink reverse osmosis filters, 1,4-dioxane was removed to concentrations below the one-in-a million risk level (0.35 μg/L) in communities served by Cape Fear River water in North Carolina. These filters are prohibitively costly for some homeowners.

I declare under penalty of perjury that the foregoing is true and correct to the best of my knowledge and belief.

Detlef Knappe, Ph.D.

4/11/18
Date

[6] *Id.*

Exhibit A

to the Declaration of Detlef Knappe, Ph.D.
in Support of Petitioners' Opening Brief

Curriculum Vitae

Name: Detlef R. U. Knappe **April 3, 2018**

I. Brief Resume

Name Detlef Knappe

1. Education background:

Ph.D., Environmental Engineering in Civil Engineering, 1996, University of Illinois, Urbana, IL.
M.S., Environmental Engineering in Civil Engineering, 1991, University of Illinois, Urbana, IL.
B.S., Civil Engineering, 1989, University of Illinois, Urbana, IL. Highest honors.

2. Professional experience:

Professor, 2008-present, NC State University, Department of Civil, Construction, and Environmental Engineering
Visiting Scholar, Spring 2013, US Environmental Protection Agency, Research Triangle Park, NC
Associate Professor, 2002-2008, NC State University, Department of Civil, Construction, and Environmental Engineering
Visiting Scholar, Fall 2005, Swiss Federal Institute of Technology (ETH), EAWAG, Switzerland
Assistant Professor, 1996-2002, NC State University, Department of Civil Engineering
Graduate Research and Teaching Assistant, 1991-1995, University of Illinois, Environmental Engineering in Civil Engineering, IL
University Fellow and Graduate Research Assistant, 1989-1991, University of Illinois, Environmental Engineering in Civil Engineering, IL

3. Scholarly and creative activities:

Refereed Activity	*Number*
Book Chapters	2
Journal Articles	48 (+1 submitted)
Research Reports	14

Non-Refereed Activity	*Number*
Conference Papers	60
Conference Abstracts	87
Invited Presentations	56

4. Membership in professional organizations

American Chemical Society, 1999-present
American Geophysical Union, 1998-2008

American Society of Civil Engineers, 1987-present
American Water Works Association, 1989-present
Association of Environmental Engineering and Science Professors, 1996-present
Engineers Without Borders, 2008-present
International Water Association, 1996-present

5. Scholarly and professional honors

Best paper award for our 2016 publication in ES&T Letters, 2017
NSF Science Nation video of our 1,4-dioxane research in the Cape Fear River watershed, 2015
Thesis advisor for the 1st place winner in the American Water Works Association Academic Achievement Award competition for the best Master's Thesis, 2013
Outstanding Teacher Award (NCSU College of Engineering), 2011
Advisor for the winner of the Best Student Paper Award at the American Water Works Association Water Quality Technology Conference, 2007
Thesis advisor for the 2nd place winner in the American Water Works Association Academic Achievement Award competition for the best Master's Thesis, 2007
AWWA Water Science & Research Division Best Poster Award, 2006
Bill Horn Kimley-Horn Faculty Award, NC State University, 2003
AWWA Water Science & Research Division Best Paper Award, 2001
Young Civil Engineer Achievement Award, University of Illinois, 2000
Thesis Advisor for the 2nd place winner in the AEESP/Montgomery Watson Master's Thesis Award Competition, 1999
University of Illinois Fellowship, 1989-1991
Bronze Tablet Recipient, University of Illinois, 1989
Ira O. Baker Prize, Department of Civil Engineering, University of Illinois, 1989
A. Epstein Award, Department of Civil Engineering, University of Illinois, 1989
Chi Epsilon, 1988-present
Tau Beta Pi, 1988-present

6. Professional service on campus

Department RPT Committee Member 2014-2016, Chair 2016-present
Global WaSH Cluster Hire Search Committee, 2015-present
Department ABET Assessment Committee for Laboratory Outcomes Member, 2001-2015, Chair 2015-present
Department EB V/Oval Lab Committee Member 2008-2010, 2016-present
Department Equipment and Facilities Committee Member 1998-2002, 2013-2016, Chair 2002-2012
WREE Group Coordinator, Fall 2011-Spring 2012
Department Head Search Committee Member, 2004 and 2009-2010
Department Awards Committee Member, 2007-2011
Department Sustainability Task Force Member, 2008-2010
WRRI Director Search Committee Co-Chair, 2008-2009
Department Compact Planning Committee Member, Spring 2007
Water Resources and Environ. Engrg. Seminar Series Teleconference Coordinator, 1998-2004
Department Faculty Search Committee Member, 1997, 1999, 2007

Department Open House Committee Chair, 1998-1999
Department Open House Committee Member, 1997-1998
Department Flower Fund Chair, 1996-1997
College Welcome Presenter, 2001
Department Representative for Summer Orientation, 1998-2000
Technical Advisory Committee Member for Engineers without Borders (NCSU Student Chapter), 2006-present

7. Professional service off campus

Committee Appointments
NC Science Advisory Board, Member, 2017-present
EPA Science Advisory Board, Member, Drinking Water Committee, 2016-present
Trustee, AWWA Water Science and Research Division, 2016-present
AEESP Lectures Committee Member, 2008-2016, Subcommittee Chair for lecturer selection at the AWWA Annual Conference, 2014-2016
AWWA Publications Award Committee Member, 2013-present
AWWA Activated Carbon Standards Committee Member, 2003-present
AWWA Regeneration Standards Subcommittee Chair, 2005-2007
AWWA Organic Contaminants Research Committee Member, 2000-2005, 2007-present
AWWA Carcinogenic Volatile Organic Compounds Working Group, 2011-2014
AWWA Particulate Contaminants Research Committee Member, 2001-2005

Journal Editorship
Topic Editor, Drinking Water Engineering and Science (Open Access Journal), 2011-present
Associate Editor, Water Science and Technology, 2009-2013

Conference Organization
Organizer for special topic session "GenX and Emerging Contaminants of Concern," NC Water Resources Research Institute Annual Conference, 2018
Organizer for special topic session "Effects of Perfluoroalkyl Substances on Drinking Water Quality and Treatment," AWWA Annual Conference, 2017
Organizer for special topic session "Water Treatment with Superfine Powdered Activated Carbon for Organics Removal," AWWA Water Quality Technology Conference, 2015
Organizer for special topic session "Activated Carbon Adsorption," AWWA Annual Conf., 2013
Co-organizer of ACS Symposium "Advances in Adsorption Processes," 2007-2008

Review
Peer reviewer for journals, conference abstracts, and research proposals (NSF, NIH, EPA, Water RF, EREF, WRRI, Research Council of Norway, U.S.-Israel Binational Science Foundation), 1991-present
Project Advisory Committee Member for WateReuse Foundation project, 2015-present
Project Advisory Committee Member for AwwaRF/Water RF research projects, 1997-2011

II. TEACHING AND MENTORING OF UNDERGRADUATE AND GRADUATE STUDENTS

A. Teaching Effectiveness

Courses Taught, Enrollment, and Student Evaluations for the Past Three Years

Semester	Course Code	Enrollment	Student Evaluations*, §
Spring 2015	CE 771	12	4.8 (4.4)
Fall 2015	CE 378	28	4.7 (4.1)
	CE 574	16 8‡	4.6 (4.5) 5.0 (4.5) ‡
Spring 2016	CE 771	6	4.3 (4.5)
Fall 2016	CE 378	30	4.4 (4.1) – partially taught by Amie McElroy, I served as her teaching mentor
	CE 574	15	4.8 (4.5)
Spring 2017	CE 771	10	4.8 (4.6)
Fall 2017	CE 378	30	4.5 (4.0)
	CE 574	19 3‡	4.1 (4.5) not evaluated
Spring 2018	CE 771	6	ongoing

* Evaluation is the average response to "Overall, the instructor was an effective teacher" with a choice of 1 through 5. A response of 5 represents "strongly agree."
§ Departmental average is shown in parentheses.
‡ Engineering Online section

Summary of Peer Evaluations of Teaching

Dates: 10/17/17, 10/19/17, and 10/22/17
Faculty Member: Detlef Knappe
Peer Reviewers: Joel Ducoste and Sankar Arumugam
Course No. and Name: CE 378 – Environmental Chemistry and Microbiology

Evaluation:

"Very well" and "Adequately" were the only boxes that were checked on the Class Observation and Course Materials Checklists (apart from "Not applicable"). *What worked well in the class*: "Good pace." "Good discussion of how to organize oral presentation." "I attended a laboratory session. The instructor started off the class reminding students of today's assignment, then helped them get started on the required measurements. The lab was well organized and appeared to be appropriately stocked with the required supplies and equipment. All students arrived promptly and were focused on their work. Everyone appeared to understand what was going on." "Attention was given to each lab group." "Good preparation for oral presentations. Good presentation, illustrations of what is good and bad was helpful. Clear review of quiz solution." *What could have been improved*: "Rework slides from others (remove big blackouts) to get students more involved in discussion." "The

instructor and several students were not initially wearing safety glasses." "Consider asking student reading newspaper to not attend class as it may set tone for others." "Perhaps write out definition of accuracy and precision and then illustrate by example." "Ask students to critique slides." Comments on course materials: " Course materials are clear and well organized. Lab experiments are clear and easy to follow. Course covers basic environmental laboratory techniques that will be useful for those that go on to do laboratory research." "Clear course description and expectations." "Well organized handouts."

B. Instructional Development

Presented a class on critiquing research papers in the CE610 Research Methods class led by Dr. Ranjithan, Fall 2015, Spring 2016, Fall 2016.

Participated in discussions that led to a new Sustainable Engineering Design course, an interdisciplinary course between CCEE and Architecture. First offered in Spring 2012. Lead: Dr. Ranjithan in CCEE and Dr. Hill in Architecture. Provide lecture on water conservation each year.

Developed course content for CE 378 (Environmental Chemistry and Microbiology). Emphasizes fundamental concepts of chemistry and microbiology as they apply to (1) characterizing water and air quality and (2) finding engineering solutions to improve water and air quality. The course integrates theory and hands-on laboratory experiments. First offered Fall 2010.

Co-developed (with Dr. Joel Ducoste) course content for CE 373, a new introductory Environmental Engineering course (Spring 2002). I am continuing to develop lecture, homework, and project materials for CE 373 to enhance the sustainable engineering content for this course. For example, students are completing group projects related to green building design and construction practices. During the summer of 2009, Joe DeCarolis, Francis de los Reyes, Morton Barlaz and I re-designed the content of CE 373; in particular, concepts of engineering for sustainability were introduced.

Revised course content for CE 374, a junior-level environmental engineering laboratory course that introduces students to analytical techniques for the assessment of water and air quality. Both through Education and Technology Fee funds and matching funds from the College of Engineering, equipment was obtained that (1) introduces students to modern analytical techniques employed in environmental engineering practice and (2) strengthens the process engineering component of this course. Using the new equipment, experiments were developed that introduced students to common unit operations in water and wastewater treatment through hands-on experiences. Formal laboratory report requirements were designed to improve students' technical writing skills, and an oral presentation component was added in the Fall 2003 semester to give students an opportunity to present experimental results in verbal form using appropriate visual aids.

Modified notes for and taught a CE 381 laboratory session on viscosimetry on a semesterly basis (Spring 1997 – Spring 1999).

Completely revised course material for CE 484, a senior-level undergraduate course that introduces students to the design of unit operations for the treatment of water and wastewater. Design concepts for both physicochemical and biological treatment processes are presented and supplemented by field trips to local water and wastewater treatment plants. In the Fall 2000 semester, I introduced a technical writing and presentation assignment that gave student groups the opportunity to research a current topic in water and wastewater treatment (e.g. algal toxins, endocrine disruptors). In their course evaluation forms, students commented nearly unanimously that they enjoyed the assignment despite nearly equally unanimous comments that the assignment represented a substantial time-commitment. By requiring student groups to complete project milestones throughout the semester, they completed this open-ended assignment effectively and with enthusiasm. I was also pleasantly surprised by the quality of the students' final papers and presentations.

Participated in an *ad-hoc* committee to revise CE 574. The course action form and syllabus were changed to expand the environmental chemistry component of this course. Over the course of the Fall 2012 and Fall 2013 semesters, I updated course content and adopted a new textbook.

Completely revised course material for CE 672 (last offered in Spring 1998, currently not offered), an advanced graduate level course that focuses on the application of mass transfer concepts for the treatment of water and waste. Covered topics include activated carbon adsorption, ion exchange, gas transfer, and membrane treatment processes.

Completely revised course material for CE 771 (formerly CE 571), a graduate level course that focuses on the application of fundamental physicochemical principles to the design of common unit processes used in the treatment of water and waste. Covered topics include sedimentation, coagulation/flocculation, filtration, oxidation/reduction, disinfection, softening, adsorption, and membrane treatment. Offered CE 771 (formerly CE 571) through the Engineering Online program to students as far away as Washington State and Qatar.

Co-developed course material for CE 796C (Environmental Behavior of Organic Contaminants), an advanced graduate level course, in which students apply principles of environmental organic chemistry to predict the partitioning of contaminants among environmental media and to model chemical and biological transformation processes. Initial offering: Spring 07.

Coordinated effort to organize graduate course offerings in the process engineering area (Spring 2003). Course action forms for CE 571, CE 574, CE 771, and CE 774 were updated, and CE 573 was added.

Attended the College of Engineering Teaching Effectiveness Workshop conducted by Richard Felder and Rebecca Brent, McKimmon Center, NCSU, August 12-14, 1996. Began to enhance my courses by (1) incorporating more group activities, (2) addressing different learning styles, and (3) developing more problems that address higher level thinking.