UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

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

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

These comments build on and incorporate by reference our groups' written and oral submissions to the Scientific Advisory Committee on Chemicals (SACC) in connection with its December 5-6, 2019 meeting to review the draft NMP evaluation.

Executive Summary

NMP's risks to workers and consumers are serious and well-documented. Extensive data establishes that acute exposure to low doses of NMP causes fetal death and chronic exposure causes reduced fertility. NMP is also known to cause neurotoxic, kidney and liver effects and has produced liver tumors in mice. NMP is extensively used in commercial and industrial applications and is a component of widely distributed consumer products. According to the draft EPA evaluation, more than 11 million workers are potentially exposed to NMP during its many industrial and commercial uses[2] and EPA has previously determined that 732,000 consumers are exposed to NMP during paint and coating removal alone.[3] The NMP-exposed

[1] 84 Federal Register 60087 (November 7, 2019); https://www.epa.gov/sites/production/files/2019-11/documents/1_draft_risk_evaluation_for_n-methylpyrrolidone_110419_public.pdf. (NMP Risk Evaluation).

[2] The NMP Risk Evaluation provides estimates of the number of potentially exposed workers for each condition of use (pp. 72-73). When added together, these estimates total over 11 million. The largest worker populations are for Application of Paints, Coatings, Adhesives and Sealants (2 million), Commercial Automotive Servicing (910,000), Soldering (4 million), and Fertilizer Application (1.3 million).

[3] 82 Federal Register 7464, 7503 (January 19, 2017) (Proposed Restrictions on Methylene Chloride and N-Methylpyrrolidone Use in Paint Removal under Section 6 of the Amended Toxic Substances Control Act). A significantly larger number of consumers is probably exposed to the consumer products addressed by the draft evaluation although EPA does not estimate the size of this population.

population includes tens of thousands of pregnant women at risk of fetal death[4] and a much larger group of men and women of child-bearing age who may experience loss of fertility from NMP exposure.

EPA issued a final TSCA Work Plan risk assessment for paint removal uses of NMP in 2015.[5] Based on that assessment, EPA determined that these products present an unreasonable risk of injury under TSCA and proposed to ban their sale for commercial and consumer use under section 6(a) on January 18, 2017.[6] Our groups were strongly supportive of EPA's proposed paint removal ban and deeply concerned when new EPA leadership failed to finalize these critical protections for workers and consumers. In the face of this delay, some of us worked successfully with leading retailers to voluntarily stop sales of paint remover products containing NMP and methylene chloride (MC).[7] These efforts are an important first step in transitioning to safe and sustainable paint removal products but do not eliminate the need for forceful regulatory action to ban NMP use under TSCA.

The draft NMP risk evaluation broadens the scope of the 2015 risk assessment to include several consumer and commercial uses of NMP in addition to paint and coating removal. The draft confirms EPA's earlier finding that NMP causes severe developmental effects and reaches the additional conclusion NMP is linked to adverse effects on reproductive performance. As EPA summarizes the extensive evidence for these effects:

> "**There is a robust dataset for the critical reproductive and developmental effects that serve as the basis for the PODs used in this risk characterization. The available studies demonstrate clear, consistent effects on a continuum of reproductive and developmental endpoints following NMP exposure across oral, inhalation, and dermal exposure routes. Each of the critical endpoints supporting the PODs represents an adverse effect that is biologically relevant to humans.** The acute POD based on fetal mortality reflects consistent observations across multiple high-quality studies using multiple exposure routes. The chronic POD selected based on reduced fertility following exposure across lifestages in a high-quality study is supported by other high-quality studies demonstrating reduced fertility in males and females exposed only as adults. The POD derived from reduced fertility is within close range of PODs derived from a developmental endpoint (fetal body weight) that is consistently observed across studies, species, and routes of exposure. **The quality of the studies, consistency of effects, relevance of effects for human health, coherence of the spectrum of reproductive and developmental effects observed and biological plausibility of the observed effects of NMP contribute to the overall confidence in the PODs identified based on reproductive and developmental endpoints."** (p. 207) (emphasis added).

The risk evaluation determines that 11 industrial and commercial uses of NMP and two consumer uses present unreasonable risks under TSCA. These include the paint and coating removal uses that would be

[4] For example, in the 2017 proposal, EPA estimated that consumers using NMP-containing paint removers included 38,000 pregnant women. 82 Fed. Reg. at 7509.

[5] https://www.epa.gov/sites/production/files/2015-11/documents/nmp_ra_3_23_15_final.pdf

[6] See note 3 supra.

[7] An integrated strategy to address NMP and MC use in commercial and consumer products is plainly the best approach to protect public health. These solvents are interchangeable for many applications. If EPA restricted one but not the other, many users would simply shift to the unregulated solvent, replacing one set of health risks with another. Indeed, as EPA's 2017 proposal notes, NMP-based products have gained sales at the expense of those using MC as a result of misleading marketing describing NMP as "green" or "bio-degradable" and implying that it is safer than MC. 84 Fed. Reg. 7466, 7503.

banned by EPA's 2017 rule[8] – reinforcing the findings of the 2017 ban proposal and the need to promptly issue a rule finalizing the ban as soon as possible. The draft risk evaluation underscores the severity of NMP's acute developmental risks, finding that "fetal resorptions (mortality) may result from a single exposure at a developmentally critical period and that, in the NMP studies reviewed by the Agency, "increased fetal mortality occurred at relatively low exposures," demonstrating a serious and imminent risk of harm. (p. 192).

Although the findings of the draft evaluation are alarming, we believe that EPA has in fact significantly understated NMP's risks because of several omissions, indefensible assumptions and errors in its risk evaluation methodology. A properly conducted risk evaluation would show that virtually all NMP conditions of use present unreasonable risks of injury and that EPA's contrary findings for 22 conditions of use are flawed and unsupportable. Of most concern is EPA's assumption that millions of exposed workers are "expected" to wear protective gloves despite the Agency's own admission that it has no evidence to support this assumption, which is contrary to workplace realities and established worker protection policies. Correcting this unfounded approach would alone require EPA to conclude that developmental and reproductive risks to workers are unreasonable across the full spectrum of NMP's many industrial and commercial uses.

In this and other areas, the draft NMP evaluation suffers from the same shortcomings as earlier draft evaluations that were strongly faulted in SACC reports. It is disappointing that the SACC's concerns and recommendations have not been heeded by the Agency and addressed in later draft evaluations for NMP and other chemicals. EPA must incorporate SACC feedback in its final evaluations. EPA's current approach to risk evaluations – as evidenced by the six draft evaluations released thus far – threaten the integrity of the TSCA program and make the Agency's actions legally vulnerable. Its actions could prevent meaningful progress on protecting the public from toxic chemicals for years to come, the exact opposite of what Congress intended when it strengthened TSCA in 2016.

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

- *The Draft Evaluation Fails to Consider Critical Endpoints for NMP and Disregards Chronic Risks to Consumers (pp, 6-11)*
    - EPA acknowledges that studies show that NMP causes neurotoxicity, liver toxicity, kidney toxicity and immunotoxicity but makes no effort to estimate the level of risk they may pose to exposed workers and consumers.
    - EPA recognizes that NMP has caused liver tumors in mice but does not discuss the significance of these findings or make any determination whether NMP poses an unreasonable cancer risk to exposed workers and consumers.
    - The draft evaluation assumes that that consumers are not at risk for reproductive effects from chronic exposure when in fact many consumers likely use NMP products repeatedly, resulting in chronic exposures that put them at risk of reproductive harm.

[8] For workers, Margins of Exposure (MOEs) for removal of paints, coatings, adhesives and sealants were determined to be below benchmark MOEs for both acute fetal mortality and chronic reproductive endpoints, in some cases even where glove use was assumed. NMP Risk Evaluation at 232-234. The same was the case for consumer paint removal use. Id., at 263.

- *EPA's Exclusion of All Environmental Releases Violates TSCA and Disregards Additional Human Exposure Pathways that Contribute to Aggregate Exposure and Risk (pp. 11-15)*

    - Removing all environmental exposure pathways from risk evaluations is contrary to the plain language and structure of TSCA and will defeat the central purpose of TSCA reform.
    - The SACC has repeatedly raised concern about EPA's failure to consider environmental pathways of human exposure.
    - The air, water and waste pathways excluded from the NMP evaluation are significant contributors to human exposure and should be included in risk determinations.

- *The Draft Risk Evaluation Fails to Account for Multiple Sources of Exposure by Consumers and Workers (pp. 15-16)*

    - EPA makes no effort to examine aggregate risk from multiple pathways, such as concurrent workplace, consumer product, and environmental exposures, which are common for many individuals and communities.
    - EPA's unexplained failure to combine multiple exposure pathways violates its obligation under TSCA and EPA regulations to use aggregate or sentinel methods of exposure assessment for determinations of unreasonable risk or justify why it is not employing them.

- *The Draft Evaluation Inadequately Addresses Risks to Vulnerable Populations and Fails to Apply Sufficient Uncertainty Factors in Calculating Benchmark MOEs (pp. 16-21)*

    - EPA's 10X Uncertainty Factor (UF) for intra-species variability is not sufficient to protect the subpopulations that EPA recognizes have greater susceptibility to NMP.
    - EPA bases its MOE for reproductive effects on the LOAEL in the Exxon two-generation study, but fails to apply the UF of 10 that EPA normally uses in the absence of a NOAEL.
    - EPA's benchmark MOEs for acute and chronic effects should include a further UF of 10 for database uncertainty to account for the lack of adequate data on developmental neurotoxicity, immunotoxicity, and endocrine effects.
    - With these adjustments, the benchmark MOE for acute effects would be 600 and the benchmark MOE for chronic effects would be 6000.
    - For endpoints that EPA believes lack sufficient data for risk determinations, it should immediately use its TSCA testing authorities to obtain the necessary information and determine whether NMP presents an unreasonable risk for those endpoints.

- *EPA's Unreasonable Risk Determinations for Workers Are Under-Protective Because They Assume Consistent Use of Protective Gloves Despite the Lack of Support for this Assumption in Workplace Practice, Law and Policy (pp. 21-25)*

    - EPA itself acknowledges that it "does not know the likelihood that workers wear gloves of the proper type and have training on the proper usage of gloves" and that it also lacks "data to justify a specific probability distribution for effective glove use for a chemical or industry."
    - In each of its reviews of draft evaluations, the SACC has raised concerns that EPA's reliance on PPE for determinations of unreasonable risk is unsupported and contrary to established principles of worker protection.
    - OSHA regulations and policy do not support EPA's claims that glove use is required at NMP-using facilities.

- Consistent with the OSHA/NIOSH "hierarchy of controls," the determinations of unreasonable risk in EPA's final risk evaluation should be based on anticipated workplace exposure levels *in the absence of PPE*.
- Without the assumption of glove use, worker risks for 24 of the 25 industrial and commercial conditions of use that EPA analyzes would be unreasonable.

- *EPA Lacks Sufficient Exposure Data to Support Proposed Findings of No Unreasonable Risk to Workers (pp. 26-27)*
  - EPA acknowledges that the workplace monitoring it relied on was limited and unrepresentative.
  - The Agency could have greatly enhanced the reliability of its assessment of worker exposure by using its TSCA authorities to obtain available worker exposure information from industry and state and federal agencies.
  - In finalizing the NMP risk evaluation, EPA should make every effort to obtain additional workplace monitoring data from OSHA, state agencies and industry and should use all available data to determine unreasonable risks to workers.

- *EPA's Determination that There Are No Unreasonable Risks to Occupational Non-Users (ONUs) Is Unsupportable (pp. 27-28)*
  - The draft risk evaluation provides virtually no details on the job functions of ONUs in NMP workplaces, how many ONUs are exposed to NMP, and the nature and duration of this exposure.
  - Instead, EPA makes demonstrably implausible assumptions that all ONUs lack dermal contact with NMP and have significantly lower inhalation exposure than workers directly handling NMP.
  - EPA must obtain more information about real-world ONU exposure scenarios or base its risk determinations on plausible default assumptions that reflect likely conditions in NMP workplaces.

- *EPA Improperly Discounts Its Own Calculations of Unreasonable Risk (pp. 28-29)*
  - EPA finds that conditions of use that have MOEs below EPA's benchmarks even where gloves are used nonetheless do not present unreasonable risks based on unspecified uncertainties.
  - In its final risk evaluation, EPA should adhere to its own unreasonable risk criteria and not reclassify risks that meet these criteria as "reasonable."

- *EPA Unjustifiably Concludes that NMP Does Not Present Unreasonable Environmental Risks and Ignores Climate Impacts (pp. 29-31)*
  - EPA lacks the data needed to evaluate NMP's ecological risks and has improperly withheld those studies that it has relied on.
  - EPA fails to account for the foreseeable effects of climate change, notwithstanding the SACC's recognition that temperature increases will influence important risk evaluation inputs, such as vapor pressure, water solubility, and Henry's law constants.

- *EPA's TSCA "Systematic Review" Method Is Deeply Flawed and Will Compromise the Quality, Validity and Protectiveness of EPA's Ongoing Risk Evaluations (pp. 31-35)*

- The TSCA method departs radically from accepted scientific principles for systematic review adopted by the Institute of Medicine (IOM), the National Toxicology Program (NTP) and EPA's Integrated Risk Information System (IRIS) and endorsed by the NAS and other peer review bodies.
- The SACC has "noted problems with both the systematic review design and consistent implementation of its protocols" and called upon EPA to make significant changes in approach.
- Thus far, the serious concerns raised by the SACC have not been addressed by EPA: at a minimum, EPA's final risk evaluations must respond fully to the SACC's comments and implement its recommendations.
- While the National Academy of Sciences (NAS) reviews the TSCA method, EPA should not use it in any of its risk evaluations but should instead apply one of the recognized systematic review methodologies.

I. The Draft Evaluation Fails to Consider Critical Endpoints for NMP and Unaccountably Disregards Chronic Risks to Consumers

A. EPA Gives Short Shrift to NMP's Non-developmental and Reproductive Health Effects

According to the draft evaluation, studies demonstrate that NMP causes neurotoxicity, liver toxicity, kidney toxicity and immunotoxicity (pp. 171-173). Although the draft evaluation describes the relevant studies, it does not develop Points of Departure (PODs) or evaluate the weight of the evidence for these endpoints. Thus, it makes no effort to estimate the level of risk they may pose for exposed workers and consumers. EPA's explanation for this approach is cryptic. It indicates that "[b]ased on the conclusions of previous assessments and a review of available studies, EPA narrowed the focus of the NMP hazard characterization to specific reproductive and developmental toxicity endpoints" (p. 169) and further explains that "[e]xposures that do not present risks based on sensitive reproductive and developmental endpoints are not expected to present risks for other potential health effects of NMP because other health effects occur at higher levels of exposure." (p. 19)

EPA took a different view of the endpoints it is now ignoring in its 2017 proposed rule for NMP paint and coating removal products. For example, it said that:

> "Exposure to NMP can cause kidney damage. This damage may result in signs and symptoms of acute kidney failure that include; decreased urine output, although occasionally urine output remains normal; fluid retention, causing swelling in the legs, ankles or feet; drowsiness; shortness of breath; fatigue; confusion; nausea; seizures or coma in severe cases; and chest pain or pressure. Sometimes acute kidney failure causes no signs or symptoms and is detected through lab tests done for another reason. Kidney toxicity means the kidney has suffered damage that can result in a person being unable to rid their body of excess urine and wastes. In extreme cases where the kidney is impaired over a long period of time, the kidney could be damaged to the point that it no longer functions. When a kidney no longer functions, a person needs dialysis and ideally a kidney transplant. In some cases, a non-functioning kidney can result in death."[9]

[9] 82 Fed. Reg. 7513.

Similarly, the proposal underscored that "[t]here are increased health risks for liver toxicity for many of the" workers exposed to NMP and "[s]ome form of liver disease impacts at least 30 million people, or 1 in 10 Americans."[10] Thus, there is no basis to conclude that the omitted endpoints are insignificant from a public health standpoint and could not present an unreasonable risk under TSCA.

EPA is wrong in presuming that it has identified the most sensitive endpoint for its dose response analysis for acute exposures. Its Point of Departure (POD) for these exposures is based on the critical effect of fetal death; that is, fetal resorptions and fetal and pup mortality. EPA describes this as a sensitive endpoint, but certainly it is obvious that many non-fatal adverse effects will occur at doses less than those that cause death. While we support the choice of a developmental endpoint as a critical effect for acute exposures, and we support EPA's determination that even a single exposure during prenatal development may lead to fetal damage or death, we urge EPA to consider the severity of the effect. Death is a severe endpoint, not a sensitive one, and EPA must acknowledge with appropriate uncertainty factors that many adverse effects will occur at lower doses. To provide protection for developmental effects that occur at doses below those causing death, a UF beyond the default intraspecies 10X factor should be applied, as EPA has previously done for other susceptible groups such as infants and children.[11]

Presenting the full range of risks for the large NMP-exposed population is important for public understanding as well as effective risk communication and management. In addition, the various NMP-related health endpoints affect different life stages and thus impact different subpopulations. For example, NMP poses reproductive and developmental risks to men and women of child-bearing age, but infants, children and the elderly would be at risk for neurotoxic, liver and kidney effects. Similarly, these latter effects may be most relevant to individuals with chronic exposure, unlike fetal mortality which is a risk for pregnant women with acute exposure to NMP. Addressing all endpoints is thus necessary to clarify how NMP exposure has different health impacts on differing segments of the population. Even groups like young adults who are at risk for multiple endpoints may have varying levels of response to NMP's toxicity. These variations in susceptibility could be overlooked if EPA's risk evaluation focuses on a subset of endpoints to the exclusion of others.

EPA should address all NMP-related health endpoints – neurotoxicity, liver and kidney effects, immunotoxicity and developmental and reproductive harm – in its final risk evaluation or provide a detailed science-based justification for retaining its current narrow approach.

B. EPA Fails to Address Evidence that NMP Causes Liver Tumors

The draft evaluation briefly describes available carcinogenicity data on NMP. (pp. 181-182) As EPA notes, Malley et al (2001) reported that:

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[10] Id.

[11] EPA, Consideration of the FQPA Safety Factor and Other Uncertainty Factors In Cumulative Risk Assessment of Chemicals Sharing a Common Mechanism of Toxicity, February 28, 2002, available at https://www.epa.gov/sites/production/files/2015-07/documents/apps-10x-sf-for-cra.pdf; U.S. EPA. Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens. U.S. Environmental Protection Agency, Washington, DC, EPA/630/R-03/003F, 2005.

> "Male and female mice administered dietary concentrations of 7200 ppm had significantly increased liver weight, significantly increased incidence of hepatocellular adenoma, and significantly increased foci of cellular alteration in the liver. At 7200 ppm, male mice also had an increased incidence of hepatocellular carcinoma while the increased incidence of hepatocellular carcinoma in female mice fell within the historical control range."[12]

Details of the study are reported in Table Apx H-7 (p. 464), where EPA notes that it considers the study to be of High Quality. It is an 18-month oral dietary GLP-compliant cancer study conducted according to OECD-451. The incidence of liver adenoma and liver carcinoma were statistically significantly increased in the high dose males and females relative to concurrent controls. This should have been considered evidence supporting the determination that NMP poses a risk of cancer.

Toxicological evidence of cancer should not be dismissed on the basis that it occurs only in the high dose group, unless it is accompanied by evidence of excessive toxicity. The EPA Cancer Guidelines state that, "effects seen at the highest doses are assumed to be appropriate for assessment . . . [unless] data demonstrate that the effects are solely the result of excessive toxicity rather than carcinogenicity of the tested agent per se"[13]. The rodent studies do not report excessive toxicity at the high doses and provide no basis for dismissal of tumor evidence at high doses.

Since about 80% of all human cancers occur in people over the age of 60, even a conventional 2-year bioassay does not have sufficient latency period to detect tumor that will occur later in life. Huff et al (2008) concludes that ceasing exposure at 2 years without monitoring tumor development for additional time cannot estimate the impact of food additives, drugs, and other chemicals on humans who die in their 70s or later. For this reason, experts do not dismiss evidence of carcinogenicity if it occurs in the high dose only – the scientific presumption is that with more time (increased latency period), tumors would become evident at lower doses.[14] That is, if the high dose causes early-life cancer, than a lower dose will cause cancer too,

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[12] https://hero.epa.gov/hero/index.cfm/reference/details/reference_id/3539913

[13] EPA 2005. Guidelines for Carcinogenic Risk Assessment at A-4. Available at https://www.epa.gov/sites/production/files/2013-09/documents/cancer_guidelines_final_3-25-05.pdf (EPA Cancer Guidelines)

[14] Bucher JR. The National Toxicology Program rodent bioassay: designs, interpretations, and scientific contributions. Ann NY Acad Sci.2002;982:198–207

Haseman J, Melnick R, Tomatis L, Huff J. Carcinogenesis bioassays: study duration and biological relevance. Food Chem Toxicol. 2001;39:739–744.

Huff J. Value, validity, and historical development of carcinogenesis studies for predicting and confirming carcinogenic risks to humans. In: Kitchin KT, editor. Carcinogenicity Testing, Predicting, and Interpreting Chemical Effects. New York: Marcel Dekker; 1999. pp. 21–123.

Huff J. Chemicals studied and evaluated in long-term carcinogenesis bioassays by both the Ramazzini Foundation and the National Toxicology Program: in tribute to Cesare Maltoni and David Rall. Ann NY Acad Sci.2002;982:208–230.

Huff J. Absence of carcinogenic activity in Fischer rats and B6C3F1 mice following 103-week inhalation exposures to toluene. Int J Occup Environ Health. 2003;9:138–146

Huff J, Jacobson MF, Davis DL. The Limits of Two-Year Bioassay Exposure Regimens for Identifying Chemical Carcinogens. Environmental Health Perspectives. 2008;116(11):1439-1442..

Huff J, Lunn RM, Waalkes MP, Tomatis L, Infante PF. Cadmium-induced cancers in animals and in humans. Int J Occup Environ Health.2007;13:202–212

Huff J, Moore JA. Carcinogenesis studies design and experimental data interpretation/evaluation at the National Toxicology Program. Prog Clin Biol Res. 1984;141:43–64

but it may take a little longer. Thus, as stated above, the EPA Cancer Guidelines do not permit dismissing cancer evidence, even if it occurs only in the high dose.

The study notes that the incidence of hepatocellular carcinomas in the female mice were within historical control values for this strain of mice. However, it would be a violation of the EPA Cancer Guidelines to dismiss the tumor evidence based on comparison with historical control data instead of concurrent control data. The EPA Guidelines are clear that, "the standard for determining statistical significance of tumor incidence comes from a comparison of tumors in dosed animals with those in concurrent control animals."[15] "Generally speaking, statistically significant increases in tumors should not be discounted simply because incidence rates in the treated groups are within the range of historical controls or because incidence rates in the concurrent controls are somewhat lower than average."[16] The concurrent control group was not flawed; the evidence of cancer in the high dose female group must be considered valid.

EPA does not discuss the significance of these findings or make any determination whether NMP poses an unreasonable cancer risk to exposed workers and consumers. No effort is made to quantify NMP's cancer risk and evaluate whether it exceeds EPA numerical benchmarks for carcinogenicity, as EPA has done for other chemicals like MC, 1,4-dioxane and 1-bromopropane.

There is no apparent reason for disregarding the Malley et al findings. While liver tumors were observed only in the high dose group, the EPA guidelines for cancer risk assessment advise that "[t]he high dose in long-term studies is generally selected to provide the maximum ability to detect treatment-related carcinogenic effects while not compromising the outcome of the study" and "tumors observed in animals are generally assumed to indicate that an agent may produce tumors in humans."[17] To the extent EPA may believe that the liver tumors reported by Malley et al may result from a mode of action (MOA) related to peroxisome proliferation that is not relevant to humans, the Agency has produced no data to support this hypothesis. The cancer guidelines underscore that "[i]n the absence of sufficiently, scientifically justifiable mode of action information, EPA generally takes public health protective, default positions regarding the interpretation of toxicologic and epidemiologic data animal tumor findings are judged to be relevant to humans, and cancer risks are assumed to conform with low dose linearity."[18] EPA applies this general principle to chemicals claimed to cause liver tumors in rodents by a PPARα-mediated mechanism, advising that "it must be clearly established that a PPARα mechanism of action (MOA) is the only contributing mechanism, and that other MOAs do not contribute significantly, before effects can be considered not relevant to humans."[19] Moreover, while the draft risk evaluation cites *in vivo* and *in vitro* studies that purport to show that NMP is non-genotoxic, EPA acknowledges that it is relying on "summaries of the unpublished genotoxicity studies" and lacks the full studies themselves despite requests to the data owners to provide them and, as a result, "did not evaluate the genotoxicity and mechanistic studies using updated data quality criteria." (p. 177).

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[15] EPA Cancer Guidelines, at 2-20

[16] Id, at 2-21.

[17] Id. at 2-15 and 2-21.

[18] Id., at 1-10 through 1-11.

[19] EPA, Proposed OPPTS Science Policy: PPARa-Mediated Hepatocarcinogenesis in Rodents and Relevance to Human Health Risk Assessments, available at http://archive.epa.gov/scipoly/sap/meetings/web/pdf/peroxisomeproliferatorsciencepolicypaper.pdf Thus, in its draft risk evaluation for MC, EPA rejected "sustained cell proliferation as an alternative MOA for methylene chloride-induced lung and liver cancer," explaining that "data were not identified suggesting a receptor-mediated mode (e.g., peroxisome proliferation resulting from PPAR-α activation; enzyme induction by CAR, PXR, or AhR activation)." (p. 266).

The final NMP evaluation must fully address the evidence of NMP carcinogenicity and make a determination of unreasonable risk for this endpoint using a linear low-dose extrapolation unless it can provide convincing evidence of an MOA that is not relevant to humans.

C. EPA Has Unjustifiably Disregarded Risks of Reproductive Harm to Consumers by Assuming They Only Have Acute Exposure to NMP

The draft risk evaluation only addresses developmental (fetal mortality) risks to consumers, ignoring potential effects on fertility on the ground that "consumer exposure is not chronic in nature." (p. 160) The rationale for this approach is EPA's assumptions that consumer exposure is limited to "a single use event which may occur over a 24-hour period" and that a "consumer uses a single product or product type." (p.159) EPA claims these are "reasonable" assumption but in fact they disregard use scenarios for consumer products that could result in repeated NMP exposure over time.

The risk evaluation identifies 12 separate categories of NMP-containing consumer products, representing 52 discrete products. (p. 140) Some of these products (adhesives, adhesive removers, paint removers, paints, arts and crafts, sealants, stains and varnishes) would be expected to be used regularly by hobbyists, artists who work at home or home renovators. Others (engine cleaners and degreasers and auto interior cleaners) would likely be used frequently by consumers who maintain and repair their own or friends' vehicles. Moreover, given the many different household functions performed by NMP-containing products, it is likely that many consumers use multiple products either simultaneously or over time.

EPA's 1-BP draft evaluation acknowledged that it is not realistic to assume that consumers are only exposed once to consumer products containing this substance in view of how these products are used:[20]

> "This assumption may result in underestimating the exposure of certain consumer users, in particular those consumers who may be do-it-yourselfers who may use products more frequently or may use more than one product within a single day. There is a medium uncertainty associated with this assumption because of the possible of underestimating exposure of frequent use or multi-product users.

The NMP draft evaluation likewise recognizes that EPA's approach "may underestimate those high intensity users such as do-it-yourselfers (DIY) that could use a product multiple times in a day" (p. 159) and that the assumption of one-time product use may "underestimate NMP exposures since NMP is also found in cosmetic products and other personal care products that could be used concurrently." (p. 160)[21] Moreover, EPA's Problem Formulation for NMP cites evidence that use of NMP-containing products in homes and buildings results in elevated levels in indoor air:

[20] 1-BP Draft Evaluation at 130.

[21] The evaluation elsewhere states that ''NMP is found in cosmetics and pharmaceutical manufacture which are regulated by the Food and Drug Administration and in pesticides (as an inert ingredient) regulated by EPA but under the Federal Insecticide Fungicide and Rodenticide Act." (p. 139) Although TSCA may not directly apply to these NMP uses, they could add to consumer exposure from TSCA-regulated uses and should be considered in determining total exposure and risk to consumers.

> "According to the Environment Canada and Health Canada Draft Screening Assessment, NMP has been monitored in indoor air samples in Canada. NMP air concentrations associated with carpet and rubber-based flooring were reported in a Canadian study on indoor air releases from building materials and furnishings. NMP also was detected in air and dust samples collected from homes during a field study in Quebec (EC/HC, 2017)."

(p. 33) Although the Problem Formulation commits (p. 58) to further "[e]valuate the indoor exposure pathways based on available data," the risk evaluation itself makes no mention of NMP levels in indoor air. If in fact elevated NMP concentrations are found in indoor air, they would represent another contributor to chronic consumer exposure, adding to direct dermal and inhalation exposure from product use.

The final risk evaluation must account for chronic consumer exposure scenarios and address NMP's reproductive risks to consumers.

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

EPA's draft evaluation excludes all human exposures from environmental releases of NMP, resulting in the absence of any consideration of environmental pathways that contribute to overall human risk exposure and risk. This approach is an unlawful interpretation of TSCA, has twice been rejected by the SACC and overlooks the widespread presence of NMP in environmental media to which millions of people are exposed.

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

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

> "EPA is not including general population exposures in the risk evaluation for NMP. As explained in the Problem Formulation for the Risk Evaluation for NMP, general population exposures were determined to be outside the scope of the risk evaluation. EPA has determined that the existing regulatory programs and associated analytical processes adequately assess and effectively manage the risks of NMP 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 not focus on those exposure pathways, but rather on exposure pathways associated with TSCA conditions of use that are not subject to those regulatory processes, because the latter pathways are likely to represent the greatest areas of concern to EPA. " (p. 21)

EPA's exclusion of environmental releases that may be subject to other laws ignore the comprehensive multi-media scope of TSCA as framed by Congress.

Under section 6(b)(4)(A), TSCA risk evaluations must determine "whether a chemical substance presents an unreasonable risk of injury to health or the environment" – a requirement that entails examining all sources of exposure to the substance and reaching a comprehensive risk determination, as opposed to piecemeal determinations for isolated pathways and uses. Similarly, section 6(b)(4)(A) provides that a risk evaluation must determine the substance's risks under "the conditions of use." This broad term spans the entire life

cycle of a chemical and is defined under section 3(4) to mean "the circumstances . . . under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of." If any of NMP's conditions of use results in air emissions or releases to water, these exposures are an essential part of the risk evaluation and must be considered by EPA, regardless of whether or not they might be addressed under other laws.

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

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

In amending TSCA in 2016, Congress sought to promote "effective implementation" of the 1976 law's objectives. See S. Rep. No. 114-67, 114th Cong., 1st Sess. (2015) at 2. At the time it strengthened TSCA, Congress affirmed that the intent of the original law—to give EPA "authority to look at the hazards [of chemicals] in total," S. Rep. No. 94-698, at 2—remained "intact." S. Rep. No. 114-67, at 7. Indeed, in a statement accompanying the law's passage, its Senate Democratic sponsors underscored that, with the expanded authorities conferred by Congress, TSCA should not be "construed as a 'gap filler' statutory authority of last resort" but "as the primary statute for the regulation of toxic substances."[22]

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

[22] Congressional Record – Senate 3517 (June 7, 2016).

TSCA's strict risk-based framework for chemical risk management is not mirrored in most environmental laws that govern releases to air, water and soil and disposal of waste. For example, the standard-setting process to establish discharge limits for chemical and other pollutants under the Clean Water Act (CWA) is technology-based and does not require the elimination of all unreasonable risk.[23] The same is true of several provisions of the Clean Air Act (CAA) that regulate emissions from new and modified stationary sources of pollution and mobile sources.[24] Even statutes that do allow for consideration of risks also direct EPA to weigh cost and other economic factors. The Safe Drinking Water Act (SDWA), for example, requires cost-benefit analysis in setting limits for drinking water contaminants, the very approach rejected in the 2016 TSCA amendments.[25] And importantly, most of these laws do not include TSCA's explicit protections for potentially exposed or susceptible subpopulations at higher risk than the general population. Equally important, even if other laws provided the high level of protection required under TSCA, they narrowly focus on single media pathways of exposure and thus would not provide the cross-media, multi-pathway assessment of exposure and risk that Congress required under TSCA.

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

In its review of the 1,4-dioxane draft risk evaluation, the SACC questioned EPA's rationale for failing to consider environmental pathways of exposure:[26]

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

The SACC added that:[27]

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

The SACC underscored that "'[g]eneral human population and biota exposure must be assessed for inhalation, ingestion, and dermal routes [and that] [d]ifferent sub-populations may have different extents of exposure, but each route must be assessed."[28] EPA's narrower approach, it said, "strayed from basic risk assessment principles by omitting well known exposure routes such as water

[23] 33 U.S.C. §1317.
[24] 42 U.S.C. §§7411,7475.
[25] 42 U.S.C. §300g-1
[26] 1,4-Dioxane and HBCD SACC Report, at 18.
[27] Id.
[28] Id.

consumption by all occupationally and non-occupationally-exposed humans as well as similar exposures to other biological receptors."[29]

The SACC review of the 1-BP similarly took EPA to task for failing to consider air emissions and other environmental releases:[30]

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

It is disappointing and troubling that the NMP evaluation ignores the SACC's explicit advice.

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

The NMP risk evaluation departs from – in the SACC's words – basic "risk assessment principles" by excluding "well-known exposure routes" for this chemical and failing to provide an "overall assessment of risks." As stated in the NMP Problem Formulation, "[r]eleases to the environment from conditions of use (e.g., industrial and commercial processes, commercial or consumer uses resulting in down-the-drain releases) are one component of potential exposure and may be derived from reported data that are obtained through direct measurement, calculations based on empirical data and/or assumptions and models."[31] For example, consumers who use NMP-based products may also be exposed to NMP air emissions, particularly if they live near emitting facilities, and may also be exposed to NMP through drinking water or proximity to waste sites. Similarly, workers exposed to NMP at their places of employment may also inhale NMP from ambient air or have dermal contact with NMP-containing products used in their homes, adding to their overall exposure. In combination, these pathways represent a significant source of exposure.

Air Emissions. According to the EPA Problem Formulation,[32] "[i]nhalation is expected to be a relevant route of exposure for the general population due to the propensity for NMP air releases from ongoing commercial and industrial activities." Because NMP is frequently used in non-enclosed processes, significant loss of vapors to the atmosphere is expected. The most recent round of reporting for the Toxics Release Inventory (TRI) showed total NMP air emissions from 280 facilities of 1,532,507 million pounds in 2017.[33] Since emissions below the TRI reporting thresholds are not captured in the TRI data-base, this figure does not reflect the emissions of the many small commercial operations that use NMP as a solvent; it thus underestimates total releases to air. NMP is not regulated as a Hazardous Air Pollutant ("HAP") under the Clean Air Act (CAA) so there are no applicable federal emission limits and no reason to expect that EPA will use the CAA to evaluate the risks of NMP air emissions and take action to reduce this source of exposure. EPA apparently lacks data on NMP ambient air concentrations but air monitoring for chemicals like MC with similar use profiles indicates that air levels are highest in urban areas with a concentration of manufacturing

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[29] Id.

[30] SACC 1-BP Report at 17.

[31] Problem Formulation of the Risk Evaluation for N-Methylpyrrolidone (2-Pyrrolidinone, 1-Methyl-), May 2018, at 31, found at https://www.epa.gov/sites/production/files/2018-06/documents/nmp_pf_05-31-18.pdf (NMP Problem Formulation).

[32] Id.at 37.

[33] NMP Risk Evaluation at 30.

and use facilities. Residents of these areas may also work at these facilities and be exposed to NMP both on the job during non-work activities.

Other Environmental Exposure Scenarios. According to the draft evaluation, roughly 9,556,874 pounds of NMP land releases were reported to TRI in 2017. (p. 30) While a significant portion of these land releases were to Class I underground injection wells and Resource Conservation and Recovery Act (RCRA) Subtitle C landfills, other types of disposal totaled 1,920,162 pounds. EPA provides no evidence that exposure and risk are insignificant for NMP releases to underground injection wells and hazardous waste landfills or that existing regulations adequately control these pathways for environmental release. Moreover, the significant amount of NMP disposed of at municipal landfills is largely unregulated and may be migrating to drinking water, groundwater and surface water. As noted in the NMP problem formulation, "NMP has been detected in industrial landfill leachate (Danish EPA, 2015). Although it is not currently subject to any proposed or promulgated water regulations, NMP has been detected in wastewater (WHO, 2001) and is included on EPA's Drinking Water Contaminant Candidate Lists (CCL) 3 and 4 because it is a suspected contaminant in public water systems that may require regulation under the Safe Drinking Water Act (SDWA)."[34]

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

In its report on the 1,4-dioxane and HBCD risk evaluations, the SACC noted EPA's failure to consider releases associated with disposal, including "the movement and breakdown of disposed materials from soils and in particular from landfills into air and waterways."[36] The findings described above confirm that these are important pathways for NMP as well. In its recent decision on the EPA framework rule for risk evaluations, the Ninth Circuit ruled that "TSCA's definition of 'conditions of use' clearly includes uses and future disposals of chemicals," as well as "spills, leaks, and other uncontrolled discharges" that may occur during facility operations or from landfills or abandoned waste sites.[37] While EPA has claimed discretion to exclude from risk evaluations conditions of use (including environmental releases) that are subject to other laws, the Ninth Circuit decision also holds that EPA lacks such discretion under its risk evaluation rule. It concludes that "we do not interpret the language in the Rule to say anything about exclusion of conditions of use" and that "[w]e therefore conclude that the challenged provisions unambiguously do not grant EPA the discretion" to remove such conditions from the scope of risk evaluations.[38]

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

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[34] NMP Problem Formulation at 36.

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

[36] Id. at 113.

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

[38] Id., at 43.

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

Exposure to NMP from air emissions and other environmental releases is not the only pathway EPA has overlooked. Given the large number of commercial and consumer uses of NMP and the large exposed population, many workers in NMP manufacturing, processing and use facilities may also be exposed to the chemical in their homes. This may occur, for example, when they perform paint removal projects or use one or more other NMP-containing household products, such as adhesives, adhesive removers, paints, arts and crafts, sealants, stains and varnishes. Workers may also do weekend work or have a side business using the same skills – and the same toxic products – as during their weekday work, thus extending their exposure time. Moreover, families of workers may have "take home" exposures, i.e. contact with the worker's contaminated clothing or skin, in addition to exposure from the direct use of consumer products. For individuals exposed to NMP in multiple settings, risks would be a function of the aggregate contribution of each route to total exposure. However, the draft evaluation looks at each exposure pathway in isolation from others, thus ignoring people with exposure to NMP both in the workplace and at home.

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

> "The Committee found that the draft risk evaluation failed to consider cumulative or aggregate exposures. It was pointed out that a worker who is occupationally exposed may also be exposed through other conditions of use in the home. Yet, these exposures are decoupled in the draft risk evaluation. The Committee was concerned that 1-BP off-gassing from insulation in home and schools is inadequately assessed, thereby underestimating exposures."[39]

EPA has used the same flawed approach for NMP.

Section 6(b)(4)(F)(ii) of TSCA requires EPA risk evaluations to "describe whether aggregate or sentinel exposures to a chemical substance under the conditions of use were considered, and the basis for that consideration." EPA has not adequately used either method of exposure analysis and has failed to explain why.

EPA's risk evaluation rule defines aggregate exposure as "the combined exposures to an individual from a single chemical substance across multiple routes and across multiple pathways" (40 CFR § 702.33). The NMP draft claims that that the Agency used an "aggregate exposure" methodology because "PBPK modeling allowed EPA to integrate aggregate exposures across routes by translating exposure concentrations into internal doses (human blood concentrations)." (p. 20) However, EPA acknowledges that it "did not consider the potential for aggregate exposures from multiple conditions of use." (p. 21) This is a key element of aggregate exposure analysis under EPA's rule, yet EPA fails to explain why it chose not to include it.

The EPA rule defines sentinel exposure as "exposure to a single chemical substance that represents the plausible upper bound relative to all other exposures within a broad category of similar or related exposures." 40 C.F.R. 702.33. EPA asserts that it determined sentinel exposures by making "estimates for consumer and occupational exposure scenarios which incorporate dermal and inhalation exposure." (p. 163) Yet these estimates did not represent a "plausible upper bound" because they focused on individual conditions of use in isolation and did not reflect all contributions to exposure from workplace, consumer use

[39] Id., at 16.

and environmental releases. A true worst case "sentinel exposure" would be one which accounts for all relevant pathways.

Whether based on "aggregate" or "sentinel" exposure assessment methods, EPA' s final evaluation should base determinations of unreasonable risk on the combined contribution of all conditions of use and pathways to individual NMP exposure. Combining all contributors to individual exposure would result in smaller MOEs for NMP's acute and chronic health effects that more realistically reflect actual risk.

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

EPA also understates NMP's risks because it fails to adequately protect vulnerable populations and does not use all necessary uncertainty factors (UFs) in calculating benchmark MOEs.[40]

A. Numerous Population Subgroups Groups Are at Increased Risk of NMP's Health Effects

The draft evaluation recognizes that "[c]ertain human subpopulations may be more susceptible to exposure to NMP than others." (p. 197) For example, "the enzyme CYP2E1 is partially involved in metabolism of NMP in humans and there are large variations in CYP2E1 expression and functionality in humans . . . The variability in CYP2E1 in pregnant women could affect how much NMP reaches the fetus, which typically does not express CYP2E1." (Id.) In addition, "[n]ewborns and very young infants are particularly susceptible to NMP exposure because they are metabolically immature. CYP2E1 is not fully expressed in children until about 90-days of age." EPA also emphasizes that "pre-existing conditions affecting the liver may also impair metabolism of NMP in some individuals" and that "[g]enetic variations or pre-existing conditions that increase susceptibility of the reproductive system, the hepatic, renal, nervous, immune, and other systems targeted by NMP could also make some individuals more susceptible to adverse health outcomes following consumer or workplace exposures."

Individuals with chronic liver or kidney disease or other systemic ailments may be at particularly high risk for organ damage or other systemic adverse effects due to the failure of these two organs to adequately filter and excrete NMP and its toxic metabolites. For example, 2-pyrrolidone (2-P) is a toxic metabolite of NMP in humans, and is described as a reproductive toxicant.[41] EPA fails to identify this metabolite in its assessment (see Section 3.2.2, p. 170 on toxicokinetics), or address the implications for risk from synergistic or compounding impacts of multiple adverse endpoints. Thus, workers or consumers at risk for developmental and reproductive effects may well also be at risk for liver and kidney damage, and vice-versa.

EPA recognizes that these groups comprise "potentially exposed or susceptible subpopulations" (PESS) for which it must make specific determinations of unreasonable risk under TSCA. Because it could not

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

[41] Carnerup MA, Spanne M, Jönsson BA. Levels of N-methyl-2-pyrrolidone (NMP) and its metabolites in plasma and urine from volunteers after experimental exposure to NMP in dry and humid air. Toxicol Lett. 2006 Apr 10;162(2-3):139-45. https://www.ncbi.nlm.nih.gov/pubmed/16321482

quantify "the extent to which any of these specific factors increases risk," EPA provided "some additional protection for susceptible subpopulations" by applying a default intraspecies uncertainty/variability factor (UF) of 10. However, this UF is customarily used by EPA to account for normal expected variations in sensitivity within the healthy population.[42] Here, by contrast, EPA has identified specific subgroups with biological characteristics that make it likely that they will experience adverse effects from NMP at lower concentrations than healthy adults.[43] To provide protection to these groups, a UF beyond the default intraspecies 10X factor should be applied, as EPA has previously done for other susceptible groups such as infants and children.[44]

We recommend that EPA apply a UF of at least 20X for intraspecies variability to account for the known susceptibility of some subpopulations to NMP's developmental and reproductive effects. This would increase the benchmark MOE for these effects to 60.

B. EPA's Failed to Apply a UF of 10 to Reflect the Absence of a NOAEL for NMP's Reproductive Effects

EPA's POD for reproductive effects was based on a 1991 two-generation study by Exxon. EPA described (p. 185) its interpretation of the study results as follows:

> "At 50 mg/kg-bw/day, the lowest dose tested, male fertility decreased 18-28% and female fecundity decreased 18-20% relative to controls. Study authors concluded that these statistically significant effects were not biologically significant at low and mid-range doses because they were "within or close to historical control ranges" and identified a NOAEL of 160 mg/kg-bw/day for reproductive effects. However, historical control data from the performing laboratory were not provided. EPA considered these significant reductions in male fertility and female fecundity relative to concurrent controls biologically relevant and identified the lowest dose tested, 50 mg/kg/day, as the LOAEL for reproductive effects."

[42] For instance, in its draft Pigment Violet 29 risk evaluation EPA used an intraspecies UF of 10 despite finding "no evidence of increased susceptibility for any single group relative to the general population." Draft Risk Evaluation for C.I. Pigment Violet 29 (Anthra[2,1,9-def:6,5,10-d'e'f']diisoquinoline- 1,3,8,10(2H,9H)-tetrone) (Nov. 2018), found at https://www.epa.gov/sites/production/files/2018-11/documents/draft_pv29_risk_evaluation_public.pdf (PV29 Risk Evaluation).

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

[44] EPA, Consideration of the FQPA Safety Factor and Other Uncertainty Factors In Cumulative Risk Assessment of Chemicals Sharing a Common Mechanism of Toxicity, February 28, 2002, available at https://www.epa.gov/sites/production/files/2015-07/documents/apps-10x-sf-for-cra.pdf; U.S. EPA. Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens. U.S. Environmental Protection Agency, Washington, DC, EPA/630/R-03/003F, 2005.

According to EPA guidance, a "UF (default 10) is typically applied to the LOAEL when a NOAEL is not available."[45] The draft NMP evaluation, however, does not apply this UF although EPA's POD for reproductive effects was derived from the LOAEL in the Exxon two-generation study.[46]

We recommend applying the full UF of 10 for LOAEL-to-NOAEL extrapolation since there is no basis for reducing it. Together with a UF of 20 for intra-species variability, this would result in a benchmark MOE of at least 600 for chronic effects as compared to the UF of 30 in the draft evaluation.

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

EPA guidance calls for application of a UF where the absence of adequate data creates uncertainty in determining a chemical's health effects:[47]

> "The database UF is intended to account for the potential for deriving an underprotective RfD/RfC as a result of an incomplete characterization of the chemical's toxicity. In addition to identifying toxicity information that is lacking, review of existing data may also suggest that a lower reference value might result if additional data were available. Consequently, in deciding to apply this factor to account for deficiencies in the available data set and in identifying its magnitude, the assessor should consider both the data lacking and the data available for particular organ systems as well as life stages."

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[45] RD and RC Review, at 4-44.

[46] In comments for the SACC review of the NMP draft and previously, industry has argued that the Exxon findings could not be replicated in three repeat studies and therefore should not be the basis for EPA's POD for reproductive endpoints. However, EPA rejected this position in the draft evaluation (p. 185):

> "EPA has reviewed summaries of these two unpublished two-generation studies (RIVM, 2013; OECD, 2007b) but data in these reports are not publicly available and EPA does not have complete access to the full reports. EPA is therefore unable to evaluate study quality or incorporate quantitative information from these studies into the dose-response assessment. A two-generation whole body inhalation exposure study in rats also found no effects on fertility or fecundity following exposure to 10, 51, or 116 ppm NMP for 6 hr/day, 7 days/week prior to mating, and during mating, gestation, and lactation (Solomon et al., 1995). However, the second-generation rats were not exposed from weaning to mating, and the F1 adults were mated with a cohort of untreated rats. In addition, there were uncertainties related to actual exposures achieved in this study."

We strongly agree that EPA should not rely on study findings unless all the relevant data are available to the Agency and the public. The NMP Producers Group's comments to the SACC indicated that the commercial value of their studies would be compromised if EPA posted the data in the NMP public docket. However, if submitted to EPA to use in carrying out its responsibilities under TSCA, the data would constitute "health and safety studies" under TSCA and could not be withheld from disclosure under section 14(b)(2). We are pleased that in its December 11, 2019 letter to NMP Producers Group, EPA recognized the application of section 14(b)(2) to these studies and rejected proposals to submit them without including them in the public document and enabling our groups and others to review them. *See* Letter from Mark A. Hartman, EPA, to Kathleen Roberts, NMP Producers Group, re: EPA Request for Submission of NMP Study Reports (Dec. 11, 2019), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0236-0043

[47] RD and RC Review at 4-44

The size of this UF can vary between 3 and 10. EPA guidance advises that "the size of the database factor to be applied will depend on other information in the database and on how much impact the missing data may have on determining the toxicity of a chemical and, consequently, the POD."[48]

Despite data raising concerns for several endpoints, critical gaps exist in understanding of NMP's human health effects. For example, the draft risk evaluation cites a study by Hass et al. (1994) that provides evidence of developmental neurotoxicity but declines to consider its findings on the ground that the "study was excluded by the systematic review process and did not go through data quality evaluation because it only used a single dose." (p. 173) EPA then explains that while "there is evidence of neurodevelopmental effects following gestational exposure to a relatively high dose of NMP," a "NOAEL for neurodevelopmental endpoints has not been identified." EPA indicates that this data gap on an important endpoint "could lead to an underestimate of risk." (p. 288)

Another endpoint for which there is evidence of concern but insufficient information for risk determinations is immunotoxicity. The draft evaluation cites two limited NMP studies conducted for other purposes indicate immune toxicity but these studies are inconclusive. (p.173) Faced with similar limited data, the IRIS assessment for MC concluded that "[c]hronic and/or repeated exposure studies evaluating functional immunity are not available and represent a data gap[49] and the EPA MC risk evaluation likewise indicated that the Agency "did not carry immune system effects forward for dose-response because epidemiological, animal and mechanistic data are limited and inconclusive." (p.380) Based on the same reasoning, the insufficiency of immunotoxicity data should be considered a data gap for NMP.

The draft risk evaluation for NMP lacks any mention of potential endocrine effects even though it is listed on the Endocrine Disruption Exchange's List of Potential Endocrine Disruptors, which "identifies chemicals that have shown evidence of endocrine disruption in scientific research."[50] The lack of endocrine effects data is another area of data insufficiency for NMP.

We recommend a UF of 10 for EPA's benchmark MOE calculation for NMP's acute (fetal mortality) and chronic (reproductive) effects.[51] This UF is warranted because the NMP data-gaps involve multiple endpoints, all of which are critical for a complete and informed determination of health risks; because the endpoint of fetal death is not sufficiently sensitive; and because available data indicates the potential for adverse effects for each endpoint.[52] **With this adjustment and the additional UFs discussed above, the benchmark MOE for acute effects would be 600 and the MOE for chronic effects would be 6000.**

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[48] Id. at 4-45.

[49] Toxicological Review of Dichloromethane (Methylene Chloride) (CASRN 75-09-2) in Support of Summary Information on the Integrated Risk Information System (IRIS) [EPA IRIS Assessment]. (EPA/635/R-10/003F). Washington, D.C. http://www.epa.gov/iris/toxreviews/0070tr.pdf U (MC IRIS Assessment), pp. 263-64.

[50] About the TEDX List, The Endocrine Disruption Exchange, https://endocrinedisruption.org/interactive-tools/tedx-list-of-potential-endocrine-disruptors/about-the-tedx-list (last visited Nov. 21, 2019). .

[51] Since available data for these endpoints is inadequate, it cannot rule out the possibility that, upon further testing, NMP's immunotoxicity or developmental neurotoxicity would produce acute and chronic effects. Thus, the UF for data-base insufficiency should apply to both exposure regimes.

[52] The IRIS assessment for MC applied a database UF of 3. MC IRIS Assessment at 196. However, based on similar considerations to those discussed in the text, we argued that a UF of 10 was more appropriate.

D. EPA's Final Evaluation Would be Incomplete and Inadequate to Comply with TSCA In the Absence of Sufficient Data to Address Whether All Endpoints Present an Unreasonable Risk of Injury

EPA's failure to develop risk estimates for developmental neurotoxicity, immunotoxicity and endocrine effects is effectively a recognition that it cannot make unreasonable risk determinations under TSCA section 6(b) for these endpoints using currently available data. Yet EPA's obligation under TSCA is to address all conditions of use, hazards and routes of exposure in its risk evaluations. Where data-gaps prevent EPA from meeting this obligation, the Agency must obtain and assess the information necessary to determine whether health effects that are now poorly characterized present unreasonable risks of injury. The proper time to take these steps is **before** EPA initiates a risk evaluation. Section 26(k) of TSCA directs EPA to base evaluations on "reasonably available" information. The preamble to EPA's risk evaluation framework rule underscores that information that either exists or "can be obtained through testing" is "reasonably available" and that the Agency may be obligated to require "data [to be] generated in response to EPA data gathering, including testing, authorities."[53] For NMP, however, EPA failed to use these authorities despite its review of the NMP data-base in its 2015 Work Plan risk assessment. Any risk evaluation that EPA now finalizes without sufficient data for all endpoints would be incomplete and inadequate to comply with TSCA's requirement to determine the unreasonable risk of injury presented by a substance as a whole. **Thus, EPA must act expeditiously to require the necessary testing under section 4 and make an unreasonable risk evaluation for the health effects it is now unable to address.**

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

As in previous risk evaluations, EPA proposes to determine that NMP's risks to workers are not unreasonable where the "expected" use of gloves would reduce exposures to levels that provide "acceptable" MOEs as compared to EPA's benchmarks. The impact of this approach is to greatly reduce the conditions of use that pose unreasonable risks to workers and thus the number of workers who would be protected under restrictions on NMP use imposed under TSCA section 6(a). However, as EPA's draft evaluations recognize and the SAAC has repeatedly underscored, this approach is not grounded in data, departs from established workplace protection policy and is contrary to the realities of worker exposure to unsafe chemicals.

On the assumption that no gloves are used or gloves are ineffective, EPA calculates MOEs for exposed workers below its benchmark MOEs for 24 of the 25 industrial and commercial conditions of use it analyzes.[54] (pp. 241-251) However, it finds that 13 of these conditions of use would have MOEs above the benchmarks if workers wear gloves and on this basis concludes that they do not present unreasonable risks of injury. The conditions of use to which these findings apply have large worker populations. For example, EPA estimates that workers engaged in soldering operations number 4 million and that 1.3 million workers are employed in fertilizer application. If EPA finalizes its determinations of no unreasonable risk, these workers would receive no additional protection against developmental and reproductive harm from NMP exposure. However, if in reality glove use is non-existent or limited, risks to exposed workers would be unreasonable according to EPA's risk benchmarks and worker protections would be required under TSCA section 6(a).

[53] 82 Fed. Reg. 33726, 33732 (July 20, 2017).

[54] The only condition of use that would not present an unreasonable risk of injury in the absence of glove use is wood preservative application. (p.248)

A. EPA Acknowledges the Absence of Real-World Evidence that Workers Exposed to NMP Wear Protective Gloves

To analyze the degree of exposure reduction from glove use, EPA used the following matrix of Glove Protection Factors (PFs):

Table 2-3. Glove Protection Factors for Different Dermal Protection Strategies from ECETOC TRA v3

Dermal Protection Characteristics	Setting	Protection Factor, PF
a. No gloves used, or any glove / gauntlet without permeation data and without employee training	Industrial and Commercial Uses	1
b. Gloves with available permeation data indicating that the material of construction offers good protection for the substance		5
c. Chemically resistant gloves (i.e., as *b* above) with "basic" employee training		10
d. Chemically resistant gloves in combination with specific activity training (e.g., procedure for glove removal and disposal) for tasks where dermal exposure can be expected to occur	Industrial Uses Only	20

For each occupational exposure scenario, EPA used "professional judgment" to select a PF and then determine whether, applying that PF, NMP exposure would be reduced to levels that provide an MOE greater than the benchmark. EPA characterized its choices of PFs for different conditions of use and exposure conditions as "what if" scenarios (pp. 69-70). Thus, EPA *assumed* the type of glove used and level of employee training provided for different worker exposure scenarios; it did not base these judgments on any documented workplace practice. In fact, for each of its risk determination for NMP's conditions of use, the Agency cautioned that it "did not find data on the use of gloves for this occupational exposure scenario" and its "assumed glove protection factor values are highly uncertain."

As EPA further explained (p. 68):

> "Overall, EPA understands that workers may potentially wear gloves but does not know the likelihood that workers wear gloves of the proper type and have training on the proper usage of gloves. Some sources indicate that workers wear chemical-resistant gloves (Meier et al., 2013; OECD, 2009a; NICNAS, 2001), while others indicate that workers likely wear gloves that are more permeable than chemical-resistant gloves (RIVM, 2013). No information on employee training was found. Data on the prevalence of glove use is not available for most uses of NMP. One anecdotal survey of glove usage among workers performing graffiti removal indicates that 87% of workers wear gloves, although the glove materials varied and were sometimes not protective; only a small fraction of these workers used gloves made of optimal material for protection against NMP and some used cloth or leather gloves (Anundi et al., 2000)."

EPA added that its "[i]nitial literature review suggests that there is unlikely to be enough data to justify a specific probability distribution for effective glove use for a chemical or industry." (Id.) Thus, in describing the limitations of its occupational exposure estimates, EPA acknowledged that the "assumed parameter values with the greatest uncertainties are glove use and effectiveness." (p. 136) Having

highlighted these uncertainties, it is hard to understand how EPA can describe widespread use of gloves by NMP-exposed workers as "expected."

Moreover, EPA recognizes that, even when worn, the actual protection that gloves provide to workers may be limited (p. 68):

> "Where workers wear gloves, workers are exposed to NMP-based product that penetrates the gloves, including potential seepage through the cuff from improper donning of the gloves, permeation of NMP through the glove material, and the gloves may occlude the evaporation of NMP from the skin."

Studies show that the effectiveness of particular glove types for NMP exposure is highly variable and depends on the specific glove material and the characteristics of the NMP-containing formulation with which it is used. Thus, "glove permeation continuous contact testing of each formulation is necessary to provide proper protection." (p. 374) However, EPA provides no evidence that industry has conducted testing to identify the best glove materials for each of the many NMP-containing products and mixtures to which workers are exposed.

In its draft evaluation for 1-BP, EPA indicates that gloves provide effective protection only "if proven impervious to the hazardous chemical, and if worn on clean hands and replaced when contaminated or compromised." (p. 180). For this reason, workplace protection programs that assure selection of impermeable gloves based on permeation data and provide worker training to assure proper glove use are essential. EPA's PFs recognize the critical importance of these factors but it lacks any data on the extent to which they are in place in workplaces where NMP is present. As a result, the PFs EPA applies to different use scenarios are nothing more than guesswork.

In fact, the nature of many NMP uses indicates that widespread and effective glove use is unlikely. Many uses involve construction trades and other small businesses with high employee turnover and worker training programs that are rudimentary or non-existent. As EPA's risk evaluation shows, the worker population in these industries is extremely large and spread over many small worksites. Thus, the odds that all or most of the 4 million workers engaged in soldering or the 1.3 million workers applying fertilizers consistently wear protective gloves that reduce NMP exposure are extremely small, yet EPA is relying on an expectation of universal glove use to justify a determination that health risks to these workers are not unreasonable under TSCA.

While EPA points out that Safety Data Sheets (SDSs) for NMP and NMP-containing products recommend gloves (p. 68), it does not provide any evidence that these SDSs are read by most employers, let alone shared with workers, or that their recommendations are consistently implemented. In fact, in its proposed 2017 rule to ban MC and NMP paint removers, EPA concluded that enhanced warnings and directions for use would not be effective because "consumers and professionals do not consistently pay attention to labels for hazardous substances; consumers, particularly those with lower literacy levels, often do not understand label information; consumers and professional users often base a decision to follow label information on previous experience and perceptions of risk; [and] even if consumers and professional users have noticed, read, understood, and believed the information on a hazardous chemical product label, they may not be motivated to follow the label information, instructions, or warnings."[55]

[55] 82 Fed. Reg. at 7445

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

In each of its reviews of draft evaluations, the SACC has repeatedly raised concerns about EPA's undue over-reliance on PPE for determinations of unreasonable risk. In its report on the PV29 draft, the SAAC noted that "the analysis in the Evaluation does not discuss or account for the fact that downstream commercial users may be oblivious to chemical risks and lack even rudimentary industrial hygiene measures."[56] Similarly, in reviewing the 1,4-dioxane evaluation, the SACC concluded that the "consensus of the Committee believes that PPE may not be consistently and properly worn, as EPA assumed"[57] and noted that "[g]love use should not always be assumed to be protective" and, if worn improperly, gloves "could actually lead to higher exposures."[58] As it concluded, "8-hour use of PPE should not be used in the risk characterization of inhaled 1,4-Dioxane. Risk estimates should be presented without the use of PPE as reasonable worst case."[59]

In the case of HBCD, the SACC noted that, "it was unreasonable to assume workers would wear PPE for entire 8-hour shifts due to underlying medical conditions, facial hair, discomfort, and other issues" and added that:[60]

> "[M]any members of the Committee believed EPA should place more emphasis on the limited likelihood that respiratory protection will be adopted without specific occupational exposure guidelines for HBCD . . . Dust exposures in the construction trades (especially residential construction) continue to represent an occupational health concern because of the many small-to-medium size operators and the use of temporary (and, not infrequently, undocumented) workers. Workers in these small-to-medium enterprises may not be likely to adopt personal protective equipment (PPE) controls, so EPA's characterization of reasonable risk relying on use of PPE is not sufficiently supported by the practical realities of many workplaces."

The recent SACC report on 1-BP provides further amplification of these concerns:[61]

> "One member noted that the Committee has now received public testimony from two former highly distinguished Occupational Safety and Health Administration (OSHA) administrators expressing concerns regarding EPA's reliance upon non-regulatory guidance and PPE to reduce risks to reasonable levels. Persons familiar with PPE use realize that nominal protection factors may not be

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[56] SACC Report on PV29 at 37.

[57] These "heightened exposures" could occur as a result of "contamination of the interior of the glove" (if workers were not properly trained in glove use and replacement) or by "acting as a reservoir" for contaminants (if the gloves were not impermeable). Such occlusion (greater penetration of the skin where contaminants build up inside the glove because it is permeable) would result in *greater* dermal exposure than in the "no glove" scenario. The Supplemental Information on Releases and Occupational Exposure Assessment document accompanying the draft MC risk evaluation calculated significantly greater dermal exposure from glove use in occluded scenarios, but these findings are not reflected in the dermal exposure scenarios on which EPA bases its actual risk determinations for MC and NMP. EPA, *Draft Risk Evaluation for Methylene Chloride (Dichloromethane, DCM), DCM Supplemental File: Supplemental Information on Releases and Occupational Exposure Assessment*, available at https://www.epa.gov/sites/production/files/2019-10/documents/16_draft_supplemental_information_on_releases_and_occupational_exposure_assessment_public.pdf

[58] SACC Report on 1,4-dioxane and HBCD, at 55.

[59] Id. at 53.

[60] Id at 118.

[61] SACC Report on 1-BP, at 30-31.

achieved in actual practice. The most recent of these comments also noted that compounds with high vapor pressures (such as 1-BP) may "breakthrough" cartridge type respirators in time frames much shorter than a work shift. Since respirators do not have real-time indicators of remaining capacity, respiratory protection failure is more likely for high vapor pressure compounds. 1-Bromopropane also is known to penetrate many glove types. This increases the likelihood of failure to select an appropriate glove."

The SACC concluded that EPA "[a]ssumptions about PPE use are likely unrealistic for many of the scenarios and so the determination of whether a condition of use results in an acceptable or unacceptable risk should be based on no PPE use, with the possible exception of in a manufacturing facility."[62]

C. OSHA Regulations Do Not Support EPA Claims that Employers Must Implement PPE

EPA has repeatedly suggested that OSHA regulations obligate employers to implement PPE where necessary to provide effective protection against chemical risks. For instance, the draft NMP risk evaluation states that "EPA expects … [that] OSHA regulations for worker protection and hazard communication will result in use of appropriate PPE consistent with the applicable SDSs in a manner adequate to protect them." (p. 335 n.1.) But OSHA regulations do not require employers to follow the recommendations in an SDS, and the preamble to OSHA's hazard communication rule expressly states that "there is no requirement for employers to implement the recommended controls."[63] Moreover, OSHA regulations give employers wide latitude to interpret evidence of workplace risks and to select worker protection measures they deem appropriate. Thus, OSHA's PPE standard requires employers to assess the hazards workers face but to provide PPE only when the employer deems such measures "necessary." [64] OSHA has not set a Permissible Exposure Level (PEL) or mandated other worker protections for NMP and it is doubtful that employers are uniformly implementing PPE or workplace controls sufficient to eliminate unreasonable risks in the absence of any legal obligation to do so.

Because of the limitations of PPE, OSHA and NIOSH manage chemical risks using the "hierarchy of controls," under which hazard elimination, substitution, engineering and administrative controls are all prioritized over the use of PPE.[65] As explained by NIOSH, "[t]he hierarchy of controls normally leads to the implementation of inherently safer systems" because chemical regulation and substitution are "more effective and protective" than PPE. EPA's own risk evaluation for 1,4-dioxane likewise recognizes that "[t]he most effective controls are elimination, substitution, or engineering controls [and that] "[r]espirators, and any other personal protective equipment. . . , should only be considered when process design and engineering controls cannot reduce workplace exposure to an acceptable level" (p 52). Thus, the SACC review of the HBCD evaluation stressed that "[m]any Committee members were concerned with the reliance on PPE or engineering controls to reduce risk, as that is contrary to the hierarchy of controls." [66]

EPA's reliance on PPE to determine that unsafe NMP exposures do not present unreasonable risks is not grounded in workplace realities and sound worker protection policy. In its final evaluation, EPA's determinations of unreasonable risk must be based on anticipated workplace NMP exposure levels in the

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[62] Id at 66.
[63] Hazard Communication, 77 Fed. Reg. 17574, 17693 (Mar. 26, 2012).
[64] 29 C.F.R. § 1910.132(a).

[65] OSH, Ctrs. for Disease Control & Prevention, updated Jan. 13, 2015, https://www.cdc.gov/niosh/topics/hierarchy/.
[66] SACC Report on 1,4-dioxane and HBCD, at 73.

absence of PPE. This would require EPA to conclude that nearly all of the estimated 11 million workers with potential exposure to NMP are at unreasonable risk of developmental and reproductive harm.

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

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

For all conditions of use, TSCA requires EPA to conduct risk evaluations based on "exposure information . . . that is reasonably available to the Administrator."[67] EPA's TSCA risk evaluation regulations define "reasonably available information" to include not only "information that EPA possesses" but also information that EPA "can reasonably generate, obtain, and synthesize for use in risk evaluations."[68] EPA has substantial authority under TSCA sections 4, 8 and 11 to require the submission of existing exposure information, and to require additional monitoring or testing to fill data gaps.[69] Thus far, however, EPA has not exercised that authority for any of its draft risk evaluations. It has also failed to ask employers to share the workplace monitoring data that they are required to preserve under OSHA regulations, or asked OSHA and other state and federal agencies to provide access to the extensive exposure information in their direct possession.

The SACC was highly critical of the adequacy of the information EPA used to assess exposure in its draft risk evaluations. As stated in the SACC's report on the 1,4-dioxane draft:[70]

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

According to its PV29 report, the SAAC "considered EPA's characterization of Environmental Releases and Exposures . . . as cursory and dependent upon sweeping generalizations that are often unsubstantiated."[71] Regarding its occupational exposure assessment, the SACC urged EPA to "clearly acknowledge that there are few data to support a confident conclusion that workers would not be exposed" to PV29 and recommended that the Agency "obtain and incorporate into the Evaluation better data and documentation from the manufacturer on conditions of use, exposures, and potential for worker exposures."[72] The SACC concluded that:[73]

> "Despite the compound having been in manufacture for decades, the Committee could find no basic information on the number of exposed workers and whether medical monitoring has historically been conducted. Implicit in the Evaluation is that 'absence of evidence is evidence of absence.' The Committee could not determine whether the population size or level of attentiveness were

[67] 15 U.S.C. § 2625(k).
[68] 40 C.F.R. § 702.33.
[69] *See* 15 U.S.C. §§ 2603(a), 2607(a), 2610(c).
[70] SACC Report on 1,4-dioxane and HBCD, at 21.
[71] SACC Report on PV29, at 16.
[72] Id at 20.

sufficient to have revealed health effects even if they exist. No evidence was provided to indicate that EPA queried other Federal or state OSHAs for information on PV29 or requested occupational hygiene or environmental release-related data from the manufacturer that are typically collected and archived."

EPA acknowledges that the monitoring data it used in the draft NMP evaluation had serious limitations:

> "Where monitoring data are available, limitations of the data also introduce uncertainties into the exposures. The principal limitation of the air concentration data is the uncertainty in the representativeness of the data. EPA identified a limited number of exposure studies and data sets that provided data for facilities or job sites where NMP was used. Some of these studies primarily focused on single sites. This small sample pool introduces uncertainty as it is unclear how representative the data for a specific end use are for all sites and all workers across the US. Differences in work practices and engineering controls across sites can introduce variability and limit the representativeness of any one site relative to all sites. Age of the monitoring data can also introduce uncertainty due to differences in work practices and equipment used at the time the monitoring data were taken and those used currently, so the use of older data may over- or underestimate exposures. Additionally, some data sources may be inherently biased. For example, bias may be present if exposure monitoring was conducted to address concerns regarding adverse human health effects reported following exposures during use." (p. 137)

EPA indicated that "the impact of these uncertainties precluded EPA from describing actual parameter distributions" and the substitutes it used "are uncertain and are weak substitutes for the ideal percentile values." (Id.) Where no monitoring data were available, EPA used "modeling approaches . . . to estimate air concentrations" but recognized that these approaches "also have uncertainties." (Id.)

The risk evaluation does not describe the efforts EPA made to overcome these limitations by seeking monitoring and other data from industry but presumably this information fell far short of what EPA could have obtained using its TSCA information collection authorities. **In finalizing the NMP risk evaluation, EPA should make every effort to obtain additional workplace monitoring data from OSHA, state agencies and industry.**

VII. EPA's Determination that There Are No Unreasonable Risks to Occupational Non-Users Is Based on Implausible Assumptions that Likely Lead to a Substantial Underestimate of Risk

EPA's lack of real-world exposure information is particularly troubling in regard to its risk determinations for occupational non-users (ONUs), a large and poorly-characterized category of workers who are exposed to NMP not because of direct involvement in NMP operations but because their job responsibilities bring them into proximity to these operations. This category can include supervisors and managers, maintenance and cleaning workers, laboratory technicians, workers in adjoining chemical production and use operations and others. The draft risk evaluation provides virtually no details on the job functions of ONUs in NMP workplaces, how many ONUs are exposed to NMP, and the nature and duration of this exposure. Nor does the evaluation break out workplace monitoring data to show exposure levels for ONUs specifically.

In the absence of this information, EPA makes a series of arbitrary assumptions about all ONU exposure scenarios and, based on these assumptions, concludes that there are *no unreasonable risks* for any ONUs exposed to NMP. As EPA explains, it assumed that "ONUs do not have direct dermal contact with liquids" and that "ONU inhalation exposures are expected to be lower than inhalation exposures for workers directly

handling the chemical substance." (p. 303) To account for this assumed difference in inhalation exposure, EPA bases its unreasonable risk determinations for ONUs on "central tendency risk estimates" rather than high-end inhalation exposure levels. (Id.) The central tendency MOEs are generally higher than the high-end MOEs by a factor of 10 or more and in all cases exceed the benchmark MOEs. By contrast, a number of high-end ONU MOEs are *below* the benchmarks and would meet EPA's criteria for unreasonable risk. (p. 252-254)

EPA's assumption that ONUs have no dermal contact with NMP is implausible. Cleaning and maintenance of NMP-contaminated equipment would unavoidably result in dermal contact, as would sampling and testing of NMP-containing process streams or products for quality control purposes. Spills and equipment leaks would also likely result in dermal contact. EPA itself acknowledges that ONUs "may have direct contact with NMP-based liquid products due to incidental exposure at shared work areas with workers who directly work with NMP, and the estimate of zero surface area contact may underestimate their exposure." (p. 137) Removing dermal exposure entirely from EPA's determination of risks to ONUs severely skews EPA's risk estimates and ignores exposure scenarios that are highly likely in real world use and handling of NMP.

Assuming that there is never high-end inhalation exposure by ONUs is likewise unsupportable since there are undoubtedly some ONU inhalation exposure scenarios that are similar in magnitude and duration to those of workers involved in direct NMP operations. For example, workers in shared work areas close to equipment emitting NMP vapors could have nearly the same level of inhalation exposure as workers using this equipment. The Agency itself acknowledges that, "[w]hen EPA does not have ONU-specific exposure data, EPA's assumption that 50th percentile air concentrations predicted for workers in these activities are a good approximation of exposure is uncertain." (Id.)

EPA must obtain more information about real-world ONU exposure scenarios or base its risk determinations on more plausible default assumptions that reflect likely conditions of exposure in NMP workplaces.

VIII. EPA Improperly Discounts Its Own Calculations of Unreasonable Risk

EPA's draft evaluation not only understates NMP's risks to workers on ONUs but unjustifiably downplays its own occupational risk determinations. EPA's general approach TSCA risk determinations calls for finding risks to be unreasonable where they fall below EPA's benchmark MOEs (for non-cancer effects) or above EPA's selected cancer benchmark (for carcinogenic effects).[74] In the draft risk evaluation, however, EPA finds that risks that meet these criteria are nonetheless reasonable, and do not warrant regulatory action under TSCA.

For example, for NMP importation, EPA states that, "[w]hile the high-end scenario risk estimates indicate risk in the absence of PPE and when expected use of PPE was considered (gloves PF = 10), given the uncertainties in the model, these were not considered unreasonable risks." (p. 305) EPA reaches an identical conclusion for repackaging during NMP processing. (p. 312) EPA doesn't explain the "uncertainties in the model" that justify disregarding MOEs below its benchmark or explain why these "uncertainties" apply to these particular conditions of use but not others with similar MOEs. It is ironic that that EPA has rejected determinations of unreasonable even where the use of gloves results in an inadequate MOE. As discussed above, there is substantial uncertainty whether gloves provide effective protection to many NMP-exposed

[74] While EPA has indicated that the benchmark MOEs are not bright lines (p. 301), the Agency has not justified overriding the benchmark MOEs for NMP on the basis of the considerations discussed in its risk evaluation.

workers or are even worn consistently. Thus, the uncertainties point in the direction of higher risk from dermal exposure, not an assumption that EPA's calculated MOEs are too low.

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

IX. EPA Unjustifiably Concludes that NMP Does Not Present Unreasonable Environmental Risks and Fails to Address Climate Considerations

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

EPA lacks sufficient data to support its conclusion that NMP presents no unreasonable risks to the environment, and it has unlawfully withheld the health and safety studies that it does have from public review.

First, EPA does not have any data on NMP's hazards to terrestrial organisms.[75] However, EPA acknowledges that terrestrial species that live "near industrial and commercial facilities that use NMP may be exposed via multiple routes."[76] In its Problem Formulation document for the NMP Risk Evaluation, EPA asserted that "based on the physical-chemical and fate properties of NMP, accumulation in these [terrestrial species] is unlikely."[77] These alleged physical properties (i.e., bioaccumulation and bio-concentration factors) are not based on observed data, however, but are instead estimated based on modeling.[78] Moreover, even chemicals with relatively low bioaccumulation and bio-concentration factors may present unreasonable ecological risk if they have significant ecotoxicity. Instead of assuming away risk based on estimated chemical characteristics, EPA should use its TSCA authority to collect or generate data on NMP's toxicity to terrestrial species.

EPA also does not have data on NMP's chronic hazards to fish. Instead, EPA simply divides the acute median lethal dose ("LC50") by 10 to develop a chronic hazard value. EPA offers no support for this acute-to-chronic ratio ("ACR"), which is highly chemical and organism dependent. A recent study of approximately 200 industrial chemicals reported a median fish ACR of 12.8, with a 90th percentile ACR of 102.4 and a maximum ACR of 1370.6.[79] In its comments on EPA's draft risk evaluation for 1-bromopropane, the Science Advisory Committee on Chemicals expressed "concern[] over the lack of chronic hazard data" for ecological receptors, and urged EPA to apply additional adjustment factors (beyond an ACR of 10) to account for this uncertainty.[80] In the absence of chronic hazard data, EPA should apply a higher acute-to-chronic ratio or additional adjustment factors here as well.

For aquatic invertebrates, EPA ignores the study showing NMP's greatest ecological toxicity. In the risk evaluation, EPA reports an EC50/LC50 of 1,107–4,897 mg/L for aquatic invertebrates, based on a 1979 study of Daphnia magna.[81] However, a 2004 study cited in the NMP problem formulation document reported an

[75] NMP Problem Formulation at 38.
[76] *Id.* at 34.
[77] *Id.* at 30-31.
[78] NMP Risk Evaluation at 57.
[79] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5044967/pdf/12302_2016_Article_84.pdf
[80] SACC Report on 1-Bromopropane at 39 ("
[81] NMP Risk Evaluation at 166.

LC50 of 1.23 ml/L for that same species, approximately 1,000 times lower than the value cited in the draft risk evaluation.[82] EPA's failure to consider that study in the draft risk evaluation resulted in an underestimate of NMP's ecological risks.

Finally, EPA has not provided public access to the studies it relied on for its environmental risk evaluation. In its draft risk evaluation, EPA writes that "subsequent to [the problem formulation document], an additional five 'Key/Supporting' citations were identified by EPA after review of the OECD HPV SIDS Document for NMP. EPA obtained the full study reports from the NMP Producer's Group (BASF and GAF)."[83] However, EPA has not published any of those studies in the public docket or otherwise made them available, leaving the public unable to verify or to critically evaluate EPA's conclusions. The links to those studies in the draft risk evaluation direct the public to EPA Health & Environmental Research Online ("HERO") websites that describe such studies as unpublished and non-peer reviewed, yet there is no means of accessing the studies or the underlying data.[84]

This withholding of health and safety studies that EPA has relied on in its draft risk evaluation violates TSCA. TSCA defines "health and safety study" as "any study of any effect of a chemical substance or mixture on health *or the environment* or on both, including … *ecological studies of a chemical substance or mixture*."[85] TSCA Section 14(b) states that health and safety studies cannot be withheld as confidential business information,[86] and in its draft risk evaluation EPA identifies no reason for its failure to disclose those studies in their entirety. Indeed, EPA has determined that human health data submitted by the exact same party (the NMP Producers Group) must be disclosed in order to be used in the draft risk evaluation, explaining that EPA "must make available sufficient information for meaningful and informed comment."[87] For the same reasons, EPA must disclose all of the ecological studies that it relied on in its draft risk evaluation and provide an additional opportunity for the public to review and comment on that data.

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

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

In its report on the draft 1,4-dioxane risk evaluation, the SACC wrote that "[a]ir temperatures in many areas of the U.S. are 40°C for prolonged times and the magnitude of elevated temperatures as well as duration are likely to increase as a function of climate change. Temperatures of this magnitude would influence vapor pressure, water solubility, and thus Henry's law constants, and these scenarios should be considered in exposures where inhalation is considered."[88] The draft NMP risk evaluation similarly fails to account for

[82] Lan, CH; Peng, CY; Lin, TS. (2004). Acute aquatic toxicity of N-methyl-2-pyrrolidinone to Daphnia magna. Bull Environ Contam Toxicol. 73(2): 392-397; *see also* NMP Problem Formulation at 39.
[83] Draft NMP Risk Evaluation at 164.
[84] *See, e.g.,* https://hero.epa.gov/hero/index.cfm/reference/details/reference_id/4259519
[85] 15 U.S.C. § 2602(8).
[86] *Id.* § 2613(b)(2).
[87] *See* n. 46 supra..
[88] Id. at 42. The report also indicated that "some [SACC] members noted that [EPA] provides an estimate of the Henry's Law constant, which reflects the distribution of 1,4-Dioxane vapors between water and air at equilibrium. However, the table does not provide the blood: air partition coefficient, which is the key parameter that an inhalation toxicologist

climate change in evaluating vapor pressure, water solubility, and air-water partition coefficients. Although these effects and other climate-sensitive risk evaluation inputs are chemical-specific, "in general, increasing temperature exacerbates chemical toxicity in animal models."[89]

In addition to affecting chemicals' physical-chemical properties, climate change is also likely to affect stream flow rates, contaminant fate and transport, human sensitivity to chemical stressors, and even the use of PPE (which can be even more burdensome in higher temperature). The latest *National Climate Assessment*, an interagency effort coordinated by the United States Global Change Research Program, warns that "the assumption that current and future climate conditions will resemble the recent past is no longer valid. Observations collected around the world provide significant, clear, and compelling evidence that global average temperature is much higher, and is rising more rapidly, than anything modern civilization has experienced, with widespread and growing impacts."[90] To the extent that specific impacts are difficult to predict, EPA may account for that uncertainty through sensitivity analyses, a broader range of temperature-related assumptions, or additional uncertainty factors. It cannot, however, ignore foreseen changes in temperatures and their impacts on the risk evaluation process.

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

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

Like previous evaluations, EPA is using "systematic review" criteria developed by the TSCA program[91] to evaluate the quality of available data on NMP. Our organizations have previously commented that the TSCA method represents a deeply flawed and unscientific approach to systematic review that will compromise the quality, validity and protectiveness of the 10 risk evaluations.[92] These concerns were summarized in a recent peer-reviewed commentary published in the *American Journal of Public Health*.[93]

"Systematic review" is a well-established approach for evaluating and integrating scientific evidence to arrive at judgments about hazard, exposure and risk. The EPA framework risk evaluation rule recognizes the need for a systematic review process in determining chemical risks under TSCA.[94] However, the TSCA

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needs to understand respiratory tract absorption." Id. at 27. In its draft risk evaluation, EPA does not provide the blood: air partition coefficient for NMP.

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

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

[91] 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

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

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

[94] 82 Fed. Reg. 33726, 33734 (July 20, 2017).

method departs radically from accepted scientific principles for systematic review adopted by the IOM,[95] the NTP[96] and EPA's Integrated Risk Information System (IRIS)[97] and endorsed by the NAS[98] and other peer review bodies.

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

The TSCA approach also focuses on one limited aspect of systematic review – study quality – but fails to address other critical elements that the Agency itself recognizes are essential for science-based risk judgments. EPA's July 2017 risk evaluation framework rule defines systematic review as a comprehensive, consistent and transparent process to "identify and evaluate each stream of evidence" and "to integrate evidence as necessary and appropriate based on strengths, limitations, and relevance."[99] Yet the TSCA document lacks any protocol for these important tasks. Experts agree that a protocol for the review needs to be established in advance of individual evaluations to eliminate the potential for bias and to assure that evidence reviews are conducted using consistent, well-defined criteria. EPA's failure to take this necessary step *before conducting risk evaluation*s has severely compromised the scientific validity of the 10 initial TSCA risk evaluations.

Recent draft risk evaluations have also been based on a "hierarchy of preferences," a new concept that was not part of the original TSCA systematic review document and has likewise not been subject to peer review or public comment. The 1-BP evaluation briefly explains this approach as follows:[100]

> "EPA's approach uses a hierarchy of preferences that guide decisions about what types of data/information are included for further analysis, synthesis and integration into the environmental release and occupational exposure assessments. EPA prefers using data with the highest rated

[95] Institute of Medicine. Finding What Works in Health Care. Standards for Systematic Review. Washington, D.C.: The National Academies Press.; 2011.
[96] National Toxicology Program. Handbook for Conducting a Literature-Based Health Assessment Using OHAT Approach for Systematic Review and Evidence Integration. In: U.S. Department of Health and Human Services, editor.: Office of Health Assessment and Translation, Division of National Toxicology Program, National Institute of Environmental Health Sciences; 2015.
[97] National Research Council. Review of EPA's Integrated Risk Information System (IRIS) Process. Washington, DC: National Academies Press; 2014.
[98] National Research Council. Review of EPA's Integrated Risk Information System (IRIS) Process. Washington, DC: National Academies Press; 2014; National Research Council. Review of the Environmental Protection Agency's State-of-the-Science Evaluation of Non Monotonic Dose–Response Relationships as They Apply to Endocrine Disruptors. Washington, DC: National Academies Press; 2014; National Academies of Sciences, Engineering, and, Medicine. Application of Systematic Review Methods in an Overall Strategy for Evaluating Low-Dose Toxicity from Endocrine Active Chemicals. Washington, DC: 2017.
[99] 40 C.F.R. 704.33.
[100] Draft Risk Evaluation for 1-Bromopropane, August 2019, at 45, available at https://www.epa.gov/sites/production/files/2019-08/documents/01._1bp_draft_risk_evaluation_hero_links_external.pdf.

quality among those in the higher level of the hierarchy of preferences (i.e. data>modeling>occupational exposure limits or release limits)."

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

As reflected in the draft MC evaluation, EPA has also updated the TSCA data quality criteria for epidemiological studies.[101] The updated criteria make it more difficult for epidemiological studies to be scored as high quality and thus limit the weight they receive in the MC evaluation, reflecting a consistent tendency by the EPA TSCA program to downplay the value of human evidence. EPA has failed to explain or justify the updated criteria.

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

- *"*The Agency rationale for developing the TSCA SR should include a comparison to other SR approaches and describe the rationale for major differences."[102]
- "The Committee discussed the need to publish peer reviewed pre-established protocols for each of the Agency's reviews prior to performing the actual risk assessment. The protocol for PV29 was created concurrently with the review, which is contrary to best practices for systematic reviews."[103]
- "The Committee noted that the TSCA SR weighted scoring system may be inappropriate if there is disagreement in the weighting of different metrics. For example, a certain study characteristic that may be a 'fatal flaw' would be weighted equally to other more minor elements. The Agency should provide justification for using a weighted scoring system and the rationale for the specific metrics used for differential weighting in its evaluation of studies."[104]
- "Regarding data integration, the Committee discussed the benefits of including a more thorough and inclusive data integration discussion in the TSCA SR for PV29 … there is a need in the Evaluation for a thorough description and outline for how all evidence and data are integrated into a final weight of evidence conclusion."[105]

[101] The completed data quality evaluation for MC epi studies using the updated criteria can be found in the Supplemental File: Data Quality Evaluation of Human Health Hazard Studies – Epidemiological Studies (Oct. 2019), https://www.epa.gov/sites/production/files/2019-10/documents/10_draft_systematic_review_supplemental_file_data_quality_evaluation_of_human_health_hazard_studies_-epidemiological_studies.pdf.Systematic Review Supplemental File.
[102] PV29 SACC Report at 26.
[103] Id. at 27.
[104] Id. at 26-7.
[105] Id. at 27.

The SACC also strongly recommended that EPA move forward with National Academy of Sciences (NAS) review of its TSCA systematic review method – a commitment on which EPA dragged its feet for months until recently signing an agreement with NAS.[106]

These concerns were forcefully underscored in the SACC review of the 1,4-dioxane risk evaluation:[107]

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

The SACC "noted problems with both the systematic review design and consistent implementation of its protocols," elaborating that:[108]

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

The SACC report further indicated that "[s]everal Committee members recommended simplifying the scoring system or adopting an existing peer-reviewed method, such as the method used by the National Toxicology Program's Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR)."[109]

The SACC report on the 1-BP draft evaluation noted "challenges in following how the studies identified for data integration during the SR were applied throughout the draft evaluation."[110] It elaborated that:

> "Members noted that studies identified for data integration were difficult to match with references cited in the bibliography. There are occasional cases where key references and data used in the risk characterization did not go through data quality evaluation (DQE) at all, although that is the Committee's expectation. Members noted that there were multiple instances where the explanation of why papers rated highly in the DQE but not used in the draft risk evaluation was missing or incomplete. The Committee identified at least one instance where a study was rated low under data quality evaluation based on a reference not being available. Committee members were able to readily obtain that reference in the public literature with a simple search. Examples such as this suggest that there is continued room for improvement in EPA's internal processes for SR. The Committee also identified several areas where corrections or additional clarification is needed."

[106] https://www8.nationalacademies.org/pa/projectview.aspx?key=51889
[107] 1,4-Dioxane and HBCD SACC Report, at 30.
[108] Id. at 31.
[109] Id.
[110] SACC Report on 1-BP, at 12.

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

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

Conclusion

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

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