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EPN Comments on Proposed list of Next 20 High-Priority Chemicals
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The Environmental Protection Network (EPN) is an organization comprised of over 450 U.S. Environmental Protection Agency (EPA) alumni volunteering their time to protect the integrity of EPA, human health and the environment. We harness the expertise of former EPA career staff and confirmation-level appointees to provide an informed and rigorous defense against current Administration efforts to undermine public health and environmental protections.

General Comments

EPA has issued for public comment a proposal to designate 20 chemical substances as High-Priority Substances for risk evaluation. This action represents the second round of identification of such substances to be evaluated in its revamped Existing Chemicals program. We urge EPA to take quick action to evaluate risks of chemicals currently on the market with documented risks to vulnerable and highly exposed populations. Designation represents the starting point in a complex multi-step process by which EPA is mandated to evaluate whether or not exposure scenarios associated with potentially unreasonable-risk chemicals in commerce should be modified or eliminated, using the Toxic Substances Control Act (TSCA) authority.

TSCA mandates clear and enforceable deadlines for EPA to evaluate existing chemicals, employing risk-based evaluations in determining whether or not a chemical poses an unreasonable risk to human health and/or the environment. TSCA Existing Chemical risk evaluations and their associated risk management decisions essentially represent a lifetime regulatory statement, given that there are many thousands of chemicals to prioritize and assess (or not) and that there is no requirement to revisit these assessments and decisions at any time (unlike the pesticide regulatory program). Therefore, the agency has an obligation to get it right the first time it conducts a risk evaluation because it's, essentially, the only time EPA will address the health and environmental effects of a chemical of concern under the TSCA regulatory umbrella. In addition, EPA's final decisions have implications preempting additional state actions.

As noted above, this is the second round of chemical selection. The first ten chemicals are currently undergoing risk evaluation. To date, draft risk evaluations for six chemicals have been issued for public comment and scientific peer review. A very troubling pattern with respect to both process and content has emerged. We have pointed out in previous comments that the "framework" rules (risk prioritization and risk evaluation) both contain serious flaws that must be addressed to fulfill the 2016 TSCA mandates. **The issues that have arisen are so serious that no risk evaluation or risk management decision can be declared complete until the flaws are remedied at the relevant stages of the process, deadlines notwithstanding.** We have included an appendix of all of our comments on these issues.

The problems:

1. Exclusion of evidence due to the use of flawed, non-peer-reviewed "TSCA systematic review" guidance to select and establish the quality of information to be used in a risk evaluation. There is no credible tool for use in integrating the evidence to reach credible, scientifically supported conclusions.

In comments submitted to the agency in August 2018 (see Appendix 1), and on several occasions since, EPN has expressed its deep concerns about the process for development and the content of the draft TSCA Systematic Review Guidance. This is a complaint shared by other public health groups. To reiterate, the guidance should not be applied in the risk evaluation of chemicals under TSCA or any other environmental statute until it has been properly evaluated and deemed to be at least as good as the Integrated Risk Information System (IRIS) systematic review process. Our concern stems not only from procedural irregularities, but also from the specifics of the guidance that we believe would result in the elimination of important evidence of public health impacts from consideration, or give these impacts only limited weight. Use of the guidance could also result in accepted scientific findings about chemical risks and regulatory controls being excluded and the weakening of public health and environmental protections. The new process for the TSCA program described in the guidance document is incomplete. It has not been developed in a transparent manner with the scientific community, and it departs significantly from accepted scientific principles for systematic review supported by the Institute of Medicine and adopted by the National Toxicology Program. In August 2018, EPN provided detailed comments in three areas: 1) EPA's failure to follow the proper procedures in developing this guidance (i.e., proposal, public comment, expert peer review and revision in response to comments/peer review before implementation); 2) on general flaws associated with the entire process as described; and 3) on critical flaws identified in assessing individual studies, using epidemiology studies as examples. (See Appendix 1 for specifics.)

EPN reiterates its recommendation that EPA continue to develop and evaluate this draft guidance by submitting it to a thorough scientific peer review and interagency review before applying it in regulatory reviews. In the meantime, EPA should use the IRIS systematic review process for evaluation of chemical risks under TSCA. The IRIS protocol can be applied immediately because it has already been peer reviewed and endorsed by the National Academy of Sciences.

2. Scoping and problem formulation: Arbitrary exclusion of exposure scenarios impacting non-worker populations that must be addressed using TSCA authority. Exclusion will continue to systematically underestimate risk.

An example of inadequate problem formulation is noted for 1,4-dioxane. EPA has dismissed consumer uses, arguing that they were not within scope for this chemical per the problem formulation; the problem formulation, however, states that such activities will be considered in the scope of the risk evaluation for ethoxylated chemicals. In 2018, EPA stated that it believed its regulatory tools under TSCA section 6(a) are better suited to addressing any unreasonable risks that might arise from these activities through regulation of the activities that generate 1,4-dioxane as an impurity or cause it to be present as a contaminant, rather than addressing them through direct regulation of 1,4-dioxane. As EPN stated in its July 2019 comments (see Appendix 2), "It is fine that EPA plans to prevent 1,4-dioxane impurities in consumer products one day, but that does not eliminate the need to account for this pathway of exposure now as part of the cumulative exposure to the general population and workers." In any case, no action has been taken on this issue, which is irresponsible and a disappointment. An additional failure has been inadequately identifying susceptible and highly exposed populations, such as pregnant women and children, as is required by law. EPA's failure in this regard could lead to underestimates of risk and incorrect determinations of "unreasonable risk."

3. Failure to determine robustness of the databases on human health and ecological hazard and exposure, and to account for any deficiencies when deriving and judging adequacy of Benchmark Margins of Exposure (MOE) and Concentrations of Concern.

Beginning with its third set of comments on Pigment Violet 29 (PV29) (see Appendix 3) and continuing in its comments on the other three chemicals (Cyclic Aliphatic Bromide Clusters (HBCD), 1,4-dioxane, and 1-Bromopropane (1-BP); see Appendices 2, 4, and 5), EPN raised the issue of the inadequate effort on the part of the agency to determine the adequacy of the databases on hazard and exposure to allow it to "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment. . . " The consequences of this are two-fold: 1) EPA has not taken advantage of its enhanced ability to identify and fill data gaps, which should be done BEFORE a risk evaluation is completed and an Unreasonable Risk determination made, and 2) EPA has failed to follow long-standing agency-wide guidance on determining the adequacy of a toxicity database when deriving and characterizing the adequacy of a Benchmark MOE. This guidance, used when deriving a Reference Dose (RfD) or Reference Concentration (RfC), also applies to identification of an acceptable MOE. Implementation of these principles at an early stage in the assessment process would have led to the conclusion that the database for assessment of human hazard was too sparse to allow for a finding to be made for PV29, 1-4-dioxane, and HCBD without application of an additional uncertainty factor (UF_D) to account for the data deficiencies in deriving the Benchmark MOE.

EPA could have saved a lot of time and effort if it had taken these steps early on. Now it is faced with a number of problems: 1) Scenarios thought to be acceptable when the UF_D was not incorporated are, in fact, not OK when deficiencies are acknowledged by application of a UF_D; 2) Either the assessment will have to be abandoned or suspended until such time as adequate data have been requested and analyzed.

4. Failure to conduct health-protective aggregate exposure and risk assessments when evaluating potential risks associated with selected Conditions of Use, by erroneously excluding exposures from scenarios that could be regulated under other statutes.

Examples of this failure include that noted above for 1,4-dioxane, which does not incorporate the potential for exposure from the consumer uses into any of the exposure scenarios included in the risk evaluation. In fact, there are similar examples in every one of the four risk evaluations we have evaluated to date. In testimony to the Science Advisory Committee on Chemicals (SACC) in August 2019 (see Appendix 6), Adam Finkel, former Regional Administrator and Director of Health Standards at the Occupational Safety and Health Administration (OSHA), expressed his concern "regarding underestimating the central tendency and reasonable worst-case work exposures." This point stems from a concern that EPA's "overall appraisal of worker exposures underestimates the extent of exposure of 1-BP. EPA has stated, as a matter of policy, that it will exclude from the exposure assessment all exposures from sources that could/would be regulated under other statutes. While it may be appropriate not to use TSCA to control exposure in scenarios better covered by other statutes, it does not absolve the agency from considering them when making a risk determination for conditions of use that are to be regulated under TSCA. It is theoretically possible that a condition of use would be deemed to present an unreasonable risk if aggregate exposure is considered, but it would not present a problem if aggregate exposure is ignored.

5. Making determinations of (No) Unreasonable Risk for workers based upon the assumption of use of personal protective equipment (PPE), rather than without it, and generally excluding findings of Unreasonable Risk for high-end exposures.

EPN initially expressed its concerns about this issue in its July 19, 2019, comments on HBCD and 1,4-dioxane (see Appendix 2), but these concerns apply universally. As stated in those comments, EPN is deeply concerned that workers will not be adequately protected under TSCA because of two policy decisions EPA has made. The first policy decision of concern appeared in the draft 1,4-dioxane risk

evaluation when the agency stated that it is "more likely to determine unreasonable risk exists for workers where risks greater than the acceptable benchmarks are identified for both central tendency and high-end exposures under the conditions of use." Where risks greater than acceptable benchmarks are identified only for workers with high-end exposures, EPA will not make the determination that unreasonable risk occurs unless there are special circumstances. This policy is problematic because the agency is not factoring in worker exposure to contaminants in drinking water or other "regulated pathways" under central tendency or high-end conditions; thus, worker exposures are being underestimated under both scenarios. The second problematic policy is that when the agency finds unreasonable risk to workers, it often dismisses that risk finding by assuming workers will use PPE the entire duration of the work activity throughout their careers, even when such equipment is not required, provided or used. This last point was demonstrated in the case of HBCD, which has no OSHA or National Institution of Occupational Safety and Health standard. EPA still overrode the risks to workers by assuming constant use of respirators and gloves. The more prudent public health approach would be to make all "Unreasonable Risk" findings based upon scenarios in which the workers are not using PPE.

6. Implementation of an out-of-sync process for solicitation of public comment and conduct of the SACC scientific peer review.

Credible and supportable regulatory decisions depend, in good measure, upon the execution of an orderly and consistent sequential process of proposal, public comment, and peer review—in that order. What we have seen to date is disorder, which the agency has attributed to the fact that the assessment of the first ten chemicals has been tangled up in the development and implementation of the rules by which the Existing Chemicals risk evaluation program would be run. EPA also attributed the lack of an orderly non-arbitrary process to complications attendant to the first chemical evaluated (PV29).

While the public comment periods for the first six chemicals have been set for one to two months or longer, their scientific peer reviews have been scheduled to occur during those comment periods, depriving the peer reviewers of the ability to consider useful and robust feedback from the interested stakeholder community during their public deliberations. This scheduling reinforces the view that the agency values meeting an arbitrary deadline for a decision over the integrity of the information and its analysis going into the decision.

The draft risk evaluations for the remaining four chemicals were originally scheduled to have completed the scientific peer review process by the end of 2019. If so, and if the public comment period is set for the preferred 90 days, that deadline is guaranteed to be missed, no matter when the SACC scientific peer review is scheduled. So what might we expect during the next round of evaluations? Given all of the process missteps in trying to meet a deadline for ten chemicals, what is the likelihood of success in the next round when 20 risk evaluations are on the schedule? EPN considers this to be pretty low.

<u>Specific Comments</u>
EPN believes that the 20 chemicals proposed for inclusion on the list of the next set of high-priority substances slated for risk evaluations represent a reasonable selection. All were cited on the 2014 Work Plan as High Priority, and no information appears to have been put forward to change that attribution.

However, Di-n-octyl phthalate (DnOP) (1,2-Benzene-dicarboxylic acid, 1,2-dioctyl ester) should be added to the list and assessed along with the other five (or seven) phthalates. It is in the 2014 Work Plan with the other phthalates on the proposed list, and there appears to be no clear rationale articulated for its exclusion. Furthermore, although the agency has not yet issued its decision on the manufacturer-initiated requests that it conduct risk evaluations for Diisodecyl phthalate (DIDP) and Diisononyl phthalate (DINP), it would

make sense to respond in the positive and add them to this list. These two chemicals are also in the 2014 Work Plan and should be assessed in concert with the other four.

What does "Assessment in concert" mean with respect to these eight phthalates? It means that the agency should abandon its stovepipe/silo approach of assessing each member of a closely related chemical class in isolation and conduct true cumulative risk assessments. EPA defines cumulative risk as "the combined risks from aggregate exposures to multiple agents or stressors" (U.S. EPA. Framework for Cumulative Risk Assessment. U.S. Environmental Protection Agency, Office of Research and Development, Center for Public Health and Environmental Assessment (CPHEA), formerly known as the National Center for Environmental Assessment (NCEA), Washington Office, Washington, DC, EPA/600/P-02/001F, 2003).

The eight phthalates, in this instance, have in common a number of toxicity endpoints of concern, each of which could be the focus of cumulative assessments. There is precedent for exercising this approach as seen in the *2008 National Academies of Science (NAS) report Phthalates and Cumulative Risk Assessment: The Task Ahead* and in the Consumer Product Safety Commission's (CPSC) July 2014 report of the *Chronic Hazard Advisory Panel on Phthalates and Phthalate Alternatives*. Some minimal effort has been extended outside of the Office of Pollution Prevention and Toxics (OPPT) to apply some of the lessons from the NAS report, but no agency-wide consensus exists on a unified approach (see, for example, Christensen KL, Makris SL, Lorber M. Generation of hazard indices for cumulative exposure to phthalates for use in cumulative risk assessment. Regul Toxicol Pharmacol. 2014 Aug;69(3):380-9. doi: 10.1016/j.yrtph.2014.04.019. Epub 2014 May 9). OPPT's sister office in OCSPP (OPP) has substantial experience with conducting cumulative risk assessments in light of the Food Quality Protection Act (FQPA) legislative mandates. It only makes sense to consult with them!

EPA (OPPT) has, in fact, articulated its own concern about these eight phthalates in its 2012 Phthalates Action Plan: "EPA is concerned about phthalates because of their toxicity and the evidence of pervasive human and environmental exposure to them. Thus, EPA intends to initiate action to address the manufacturing, processing, distribution in commerce, and/or use of these eight phthalates. EPA intends to take action as part of a coordinated approach with the Consumer Product Safety Commission (CPSC) and the Food and Drug Administration (FDA)." There has been little evidence of action by OPPT up until this point in time. It is past time to see some movement on this class of chemicals.

Also on the proposed list of 20 high-priority chemicals are two sets of isomers: o-Dichlorobenzene and p-Dichlorobenzene, and 1,1-Dichloroethane and 1,2-Dichloroethane. These two pairs should also, obviously, be subjected to both aggregate and cumulative risk evaluations.

Lastly, with regard to formaldehyde, an EPA IRIS draft hazard assessment for this chemical was conducted and revised in response to peer review and public comments. It should be utilized, with minimal or no alteration, as the hazard component of the TSCA risk evaluation.

APPENDIX 1
ENVIRONMENTAL PROTECTION NETWORK COMMENTS
"Application of Systematic Review in TSCA Risk Evaluation"
August 16, 2018

Introduction

The Environmental Protection Network (EPN), a volunteer organization of EPA alumni and others who work to preserve the nation's bipartisan progress toward clean air, water, land and climate protections, believes that the process followed to develop the TSCA systematic review process is seriously flawed. The guidance should not be applied to the risk evaluation of chemicals under TSCA or any other environmental statute until it has been properly evaluated and deemed to be at least as good as the Integrated Risk Information System (IRIS) systematic review process. Our concern stems not only from procedural irregularities, but specifics of the guidance that we believe would result eliminate important evidence of public health impacts from consideration, or give these impacts only limited weight. Its use could also result in accepted scientific findings about chemical risks and regulatory controls being reversed, and the weakening of public health and environmental protections.

TSCA requires that EPA make decisions about chemical risks based on the "best available science" and the "weight of the scientific evidence." EPA's risk evaluation rule (40 CFR Section 8702.33) defines "weight of the scientific evidence" as a "systematic review method, applied in a manner suited to the nature of the evidence or decision that uses a pre-established protocol to comprehensively, objectively, transparently, and consistently identify and evaluate each stream of evidence, including strengths, limitations, and relevance of each study and to integrate evidence as necessary and appropriate based upon strengths, limitations and relevance." EPN is greatly concerned that EPA has released for public comment a new systematic review process for TSCA that does not build on the four years of progress in developing the IRIS systematic review process that has been endorsed by the National Academy of Sciences.[1] The new process for the TSCA program described in the guidance document is incomplete, has not been developed in a transparent manner with the scientific community, and departs significantly from accepted scientific principles for systematic review supported by the Institute of Medicine and adopted by the National Toxicology Program.[2,3]

Several critical steps are missing from the process to adopt the "TSCA systematic review" approach. We provide the Benchmark Dose (BMD) methodology as an example of how the review process should be undertaken. In the case of BMD, EPA conducted research, held workshops, published scientific papers, sought public comment, created public domain software for practitioners to use, and wrote guidance

[1] National Academies of Sciences, Engineering, and Medicine. Progress Toward Transforming the Integrated Risk Information System (IRIS) Program: A 2018 Evaluation. Washington, D.C.: The National Academies Press; 2018.
[2] Institute of Medicine. Finding What Works in Health Care. Standards for Systematic Review. Washington, D.C.: The National Academies Press; 2011.
[3] 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.

documents – all under the auspices of the appropriate external scientific peer review process. The EPA BMD methodology is now recognized internationally because of the thorough vetting of the approach in the scientific and regulatory community. In contrast, this draft TSCA guidance has not been the subject of workshops, scientific papers, or external scientific peer review.

EPN provides specific comments in three sections below: 1) on EPA's failure to follow the proper procedures in developing this guidance, 2) on general flaws associated with the entire process as described, and 3) on critical flaws identified in assessing individual studies, using epidemiology studies as examples. (Appendix H of EPA's guidance).

1. Procedural Failures

This TSCA guidance qualifies as a "Highly Influential Scientific Assessment" as defined in the EPA Peer Review Handbook, and as such should have been subject to a comprehensive external peer review with public participation.[4] The fact that it departs substantially from current recommendations on systematic review principles indicates that the TSCA guidance is a novel approach requiring an expert panel to evaluate its scientific validity. In addition, a cross-program EPA review should have taken place under the agency's Action Development Process so that the TSCA process could have been compared to and evaluated with accepted scientific principles of systematic review. Following that rigorous internal EPA review, a federal interagency review should have been conducted under Executive Order 13422 to allow the National Toxicology Program's systematic review experts, among others, to critique the draft TSCA approach. Since none of these reviews were conducted on this draft guidance, it was inappropriate to use this guidance to evaluate the 10 chemicals currently undergoing TSCA review, as well as chemical reviews conducted under other environmental statutes.

The risk evaluation rule requires that a systematic review for these purposes "use[s] a pre-established protocol to comprehensively, objectively, transparently, and consistently identify and evaluate each stream of evidence." This draft guidance does not meet this criterion; therefore its use in evaluating the 10 TSCA chemicals is in clear violation. It also raises the question of why the existing IRIS systematic review process was not used.

2. Guidance Flaws

EPN describes three critical flaws in the draft TSCA guidance: 1) failure to include protocols or guidance to synthesize evidence within each of the seven evidence domains, and to combine the evidence from all domains into a coherent summary, 2) use of an arbitrary quantitative scoring system for assessing individual studies, with no validation, and 3) failure to adopt adequate implementation procedures for conducting the systematic review. EPN also describes how one of the agency's systematic review processes (used for IRIS) has none of these critical flaws.

   a. The TSCA guidance fails to include a protocol for synthesizing the body of evidence selected for inclusion in the systematic review

[4] U.S. Environmental Protection Science and Technology Council. Agency Peer Review Handbook 4th Edition; October 2015.

The Institute of Medicine identified five steps in conducting systematic reviews: 1) formulating the topic, 2) developing the systematic review protocol, 3) finding and assessing individual studies, 4) synthesizing the body of evidence, and 5) providing a detailed comprehensive final report.[5] The TSCA draft guidance document acknowledges all five steps but provides details only for steps one through three, focusing most heavily on assessing individual data sources and studies for inclusion in a systematic review. The TSCA guidance on "Data Integration and Summary of Findings" (p. 26) states that this critically important step will be done but provides no information on how it will be done. The TSCA guidance lacks any protocol for determining the strengths and relevance of the selected individual studies, grouping them into streams of evidence from each of the seven domains, and integrating the findings from all domains into a coherent summary with a set of judgments about the weight of the evidence as a whole. This omission of critical steps in systematic review disqualifies the guidance from use because it does not meet the TSCA risk evaluation rule requirement; the systematic review must use a pre-established protocol "to comprehensively, objectively, transparently, and consistently identify and evaluate each stream of evidence, including strengths, limitations and relevance of each study and to integrate evidence as necessary and appropriate based upon strengths, limitations and relevance."

While the IRIS Handbook is in the process of being updated to describe in detail its systematic review process, EPA presented the key elements to the National Academy of Sciences at a workshop on February 1-2, 2018. Unlike the TSCA draft guidance, the IRIS systematic review process covers all five steps identified by the Institute of Medicine. The IRIS approach applies the principles of systematic review to identify pertinent studies of animal and human health effects, to evaluate the strengths of study methods and quality, to synthesize the body of evidence, to integrate evidence for each health outcome, and to select studies for derivation of toxicity values. The IRIS systematic review process for TSCA chemical risk evaluations would provide a more comprehensive approach than use of the incomplete draft TSCA guidance.

b. <u>The guidance uses an arbitrary quantitative scoring system for assessing individual studies</u>

The second critical flaw in the draft TSCA guidance is the use of an arbitrary and untested numerical scoring system which assigns, based on the professional judgment of one or two reviewers, numerical values for quality domains and then sums up those values to decide whether a study is high, medium, low, or unacceptable quality. None of the widely accepted systematic review methodologies in use today employ numerical scoring systems, and both the Cochrane Collaboration and National Academy of Sciences (NAS) recommend strongly against such scoring systems because they are arbitrary and not science-based.[6,7] The Cochrane Collaboration, founded in 1993, is an international non-profit, independent organization which includes the world's most authoritative expertise on systematic review methods. The Cochrane Collaboration warns that calculating a score involves choosing appropriate weights for each subcomponent

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

[6] Higgins, JPT, Altman, DG, Sterne, JAC. Chapter 8: Assessing risk of bias in included studies. In: Higgins, J, Green, S, editors. Cochrane Handbook for Systematic Reviews of Interventions Version 510 [Updated March 2011]: The Cochrane Collaboration; 2011. https://us.cochrane.org

[7] National Research Council. Review of EPA's Integrated Risk Information System (IRIS) Process. Washington, D.C.: National Academies Press; 2014.

of a study, and such scaling is nearly impossible to justify. The NAS explains that in order to assign a scientifically justified measure the reviewer would have to know how much each risk of bias domain contributes to study quality, and the domains would have to be independent of each other. The Cochrane Collaboration further explains that scoring systems inappropriately mix criteria that assess risk of bias with criteria that reflect the quality of reporting. That is a concern with this TSCA guidance, which lacks any commitment to request additional information from the authors of relevant studies, only mentioning that such requests might be made after the initial screen of the literature. Risk of bias reflects study-design characteristics that can introduce a systematic error that might affect the magnitude and even the direction of the apparent effect. Potential biases must be assessed to determine how confidently conclusions can be drawn from a study. A critical flaw of the draft TSCA guidance is its focus on reporting limitations that do not negate a study's value in demonstrating health risks. A study might be well designed to eliminate bias, which would make it valuable for consideration; however, because the study failed to report details in the publication under review the TSCA guidance would assign it a low score or deem it unacceptable. Reporting requirements are known to vary among technical journals which have different allowances for details based on the expected audience and space limitations. The TSCA scoring system for study quality and the formula for calculating a composite score lack empirical support, nor have they been evaluated or "ground truthed," as is the common practice in developing scoring approaches.

EPN notes that the IRIS systematic review process followed the recommendations of the National Academy of Sciences and does not include a numerical scoring system.[8] Instead, the IRIS approach provides detailed criteria for assessing the quality of data sources and studies, which are appropriately focused on identifying the risk of biases rather than reporting limitations. For example, IRIS evaluation of epidemiology studies is based on the Cochrane risk of bias approach, modified for environmental and occupational exposures.[9] While the IRIS systematic review process identified similar domains for epidemiology studies as the draft TSCA guidance, the IRIS approach deems a study unacceptable only when there is a bias that would produce a substantive change in the estimated effect estimate.

c. <u>The guidance fails to adopt adequate implementation procedures for systematic reviews.</u>

The third critical flaw in the TSCA draft guidance is the failure to adopt adequate implementation procedures for the systematic review. The Cochrane Collaboration requires that at least two reviewers with appropriate expertise assess each study to minimize bias, and recommends that a conflict resolution process include an additional reviewer to resolve differences in ratings between the reviewers. The draft TSCA guidance does not identify the expertise needed to review studies in any of the seven topics for which it provides a numerical scoring system: physical-chemical properties; environmental fate; occupational exposure and release; exposures to the general population, consumers and the environment; ecological hazard studies; animal toxicity and *in vitro* toxicity; and epidemiology studies. Further, the guidance states that only one or at most two reviewers will be employed at any phase of the review, and it is vague about conflict resolution among reviewers, indicating only that the reviewers will seek consensus. A further concern about implementation procedures is the lack of emphasis on the need to query authors for

[8] NRC 2014.

[9] Sterne, Hernan, et al. ROBINS-I: a tool for assessing risk of bias in non-randomized studies of interventions. BMJ 2016; 355: i4919.

additional information if necessary data are not reported in the publication under review. It should be standard practice that EPA give authors of relevant studies an opportunity to provide additional information beyond that provided in a publication. EPN notes once again that the IRIS systematic review process does not suffer from any of these implementation failings. It is clear in that process that a minimum of two reviewers will be used with appropriate expertise, and it is standard practice to ask authors of relevant studies to provide additional information if needed to evaluate the study quality and risk of bias.

3. Flaws in TSCA guidance that could eliminate reliable and relevant data from inclusion in systematic review

EPN believes that the application of this draft TSCA guidance will result in the exclusion of quality research in all seven of the topic areas covered. We provide detailed comments below on the evaluation of epidemiologic studies, as we believe this area may be the most affected.

The draft guidance provided for assessing epidemiologic studies is intended to cover the following study designs: controlled exposure, cohort, case-control, cross-sectional, and case crossover. Studies are to be evaluated in six data quality domains: study participation, exposure characterization, outcome assessment, potential confounding/variability control, analysis, and other/consideration for biomarker selection and measurement. Each of the six domains is evaluated using two to seven metrics for a total of 19 metrics. In addition, differential weights are assigned to each metric. According to the guidance, studies with even one metric scored as unacceptable will be excluded from use in a chemical's risk evaluation.

a. General comment on scoring

The assignment of equal weight to each of the "evaluation domains" is arbitrary and not based on evidence. Within each category, the assignment of "metric weighting factor" is also arbitrary, and each metric is limited to two values (X or 2X) (a similar scheme is used for the animal and in vitro studies), with the values dependent on the number of metrics in the category. The validity of this approach is untested and, given the arbitrary input values, may or may not be an accurate reflection of study quality. Also, the metrics mix study quality and reporting quality, as noted earlier, is discouraged by other systematic review expert advice.

b. General comment on information missing from published reports

The reasons for "unacceptable" ratings for nearly all items include information "not reported." While the possibility of contacting authors to obtain additional information is mentioned in the body of the report, there is no acknowledgment in the tables of such filling in of information. There are many reasons for information not to appear in a published report but to be nonetheless available. If the aim is to base decisions on the totality of the reliable evidence, considerable effort should be placed on filling in gaps where possible. (See earlier discussion of this point.)

c. Comment on using STROBE criteria for reporting

Many of the criteria for epidemiologic studies cite the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement. STROBE provides widely respected guidance on the

reporting of the types of observational studies that could be included in TSCA reviews. The STROBE developers state:

> We emphasize that the STROBE Statement was not developed as a tool for assessing the quality of published observational research. Such instruments have been developed by other groups and were the subject of a recent systematic review [28]. In the Explanation and Elaboration paper, we used several examples of good reporting from studies whose results were not confirmed in further research--the important feature was the good reporting, not whether the research was of good quality.[10]

This clarifies the distinction that the STROBE criteria relate to the quality of study *reporting*, but not necessarily the quality of the *research*. Appreciation of this distinction is lacking in guidance document. EPN is not opposed to considering the quality of reporting, but we do not believe that a missing data item should form the basis for excluding studies. Also, using these criteria are likely to handicap older studies that precede the 2007 publication of the STROBE criteria.

d. Comments on Study Participation

The evaluation domains and metrics listed are generally appropriate, but are not well differentiated or explained. These examples illustrate problems in the "study participation" evaluation domain.

i. Three metrics are listed under "study participation": participant selection, attrition, and comparison group. However, the comparison group are also participants and should be subsumed under participant selection, leaving just two categories. This would affect the arbitrary scoring in this category. If the authors intended to separate cases and controls, or exposed and unexposed into two metrics, they should state this clearly. This does not appear to be the case. This error may suggest a lack of understanding of the variety of epidemiologic study designs.

ii. "Participant selection" is chosen as one of the critical metrics, with this given as the rationale:

> The participants selected for the study must be representative of the target population. Differences between participants and nonparticipants determines the amount of bias present, and differences should be well-described. (Galea and Tracy 2007)

This is presented as a critical metric for "participant selection." We agree that participants (cases/controls, exposed/unexposed, exposed vs. unexposed time periods for case-crossover studies) should be carefully selected for all study types. Bias, however, as suggested in the second sentence, is a result of many factors, not just "nonparticipants." The paper referenced as support for this metric is largely about participants and

[10] Elm, E. Von, Altman, D. G., Egger, M., Pocock, S. J., Gøtzsche, P. C., & Vandenbroucke, J. P. (2008). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement : guidelines for reporting observational studies, *61*, 344–349. https://doi.org/10.1016/j.jclinepi.2007.11.008

nonparticipants in surveys and prospective studies, which make up only a portion of the study types (e.g., most studies relying on retrospective records would not have "nonparticipants," but still be subject to bias, which should be assessed). This also suggests a lack of appreciation for the differences among epidemiologic study designs.

e. Comments on Potential Confounding/Variability Control

i. "Variability control" is not a standard epidemiologic term, suggesting a possible lack of familiarity with epidemiologic terminology. It should be defined, deleted, or changed to a meaningful term.

ii. Two of the three metrics in this evaluation domain are the same or similar: Co-exposure Confounding/Moderation/Mediation and Covariate Adjustment. The point of covariate adjustment is to reduce or eliminate bias or confounding from any source. A covariate may be a personal characteristic, an exposure, or some other feature. Without further explanation, it would be difficult to apply these metrics independently.

Conclusion

EPN recommends that EPA continue to develop and evaluate this draft guidance and commit to submitting it to a thorough scientific and interagency review before applying it in regulatory reviews. EPA should use the IRIS systematic review process for evaluation of chemical risks under TSCA, including for the 10 chemicals currently under consideration. The IRIS protocol can be applied immediately because it has already been peer reviewed and endorsed by the National Academy of Sciences.

Respectfully submitted,

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These comments were prepared by Betsy Southerland, Hellen Gelband, Robert Kavlock, Trish Komen, and Rita Schoney, on behalf of the Environmental Protection Network. Questions should be addressed to Betsy Southerland, easydee420@gmail.com.

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APPENDIX 2

EPN Comments for the Public Meeting of the Science Advisory Committee on Chemicals Regarding Draft HBCD & 1,4-Dioxane Risk Evaluations Under the TSCA

July 19, 2019

The Environmental Protection Network (EPN) is an organization comprised of over 450 U.S. Environmental Protection Agency (EPA) alumni volunteering their time to protect the integrity of the agency, human health and the environment. We harness the expertise of former EPA career staff and confirmation-level appointees to provide an informed and rigorous defense against current administration efforts to undermine public health and environmental protections.

EPN is submitting these general comments to the Science Advisory Committee on Chemicals (SACC) to aid in their review of the Cyclic Aliphatic Bromide Cluster (HBCD) and 1,4 Dioxane draft risk evaluations during their scheduled meeting on July 29 – August 2, 2019. HBCD is mainly used as a flame retardant, and studies show it may affect human reproduction and development. 1,4-Dioxane is a solvent that is used mainly in the manufacture of other chemicals. Short-term exposure can cause eye, nose and throat irritation; exposure to large amounts may cause kidney and liver damage.

EPN expects to prepare more detailed comments on these two draft risk evaluations by the August 30 deadline but was concerned that the SACC will have concluded their review before the public comment period closes. As a matter of policy, EPN finds it extremely disingenuous to have the SACC meeting prior to the deadline for the comments, a reversal of the way EPA normally does things. This approach indicates that a) the arbitrary deadline for a decision is more important than the information going into the decision making or b) this is a mechanism to discourage the comments of the citizenry that desire to see a standardized risk evaluation process followed, or both.

EPN is focusing these initial comments on the most critical policy issues that affect not only these two chemicals but all future chemical risk evaluations under the Toxic Substances Control Act (TSCA).

EPN has the following policy concerns regarding the draft risk evaluations for HBCD and 1,4 Dioxane:

1) continued use of the flawed TSCA systematic review process to identify the key studies and synthesize the weight of evidence for each type of data and the body of information overall;
2) exclusion of pathways of exposure which could be regulated by other environmental statutes;
3) focus on worker risks primarily under central tendency conditions;
4) assumption that Personal Protective Equipment (PPE) will eliminate all worker risks even when there are no requirements for such protection;
5) failure to evaluate the risks of consumer products containing 1,4-Dioxane; and
6) analysis and inclusion of threshold cancer risk model for 1,4-Dioxane previously found unsupportable.

EPN and many other organizations submitted persuasive reasons why the problem formulations should not exclude pathways of exposure which could be regulated under environmental statutes such as the Clean Air Act (CAA), Safe Drinking Water Act, Clean Water Act (CWA) and Resource Conservation and Recovery Act (see Appendix 7). Standards and non-regulatory guidance established under these other programs may be years out of date, may be technology-based rather than risk-based, and may not be complied with at all times or in all locations. In addition, these pathways add to the cumulative risk of highly exposed people such as workers or residents near the fence line of point sources and should be added to their exposures. In the draft risk evaluation, EPA ignored those comments and refused to evaluate risks to the general public, including children and pregnant women, because these other statutes "adequately assess and effectively manage risks from 1,4-dioxane." EPA cannot justify the failure to consider drinking water contamination when there is no drinking water standard currently established for this chemical, which occurs in ground water and surface water. In addition, ambient air levels of this contaminant must be taken into consideration, even though there is an established standard in order to evaluate the cumulative exposure from all pathways. A comprehensive analysis of all pathways of exposure under TSCA may lead to recommendations that a drinking water standard or an air standard should be promulgated or updated rather than a restriction placed on a chemical's use via an action under TSCA. Recommendations for action under another statute should be seen as an appropriate end result of a TSCA evaluation and is consistent with Section 9 of TSCA, which directs the Administrator "to coordinate actions taken under TSCA with actions taken under other federal laws administered by EPA, such as the CAA and CWA. If risk is already managed *effectively* (emphasis added) under a different statute, regulation under TSCA is not necessary." This section indicated that TSCA evaluations should include an assessment of these exposure scenarios so that a decision can be made on the need for action under these other statutes.

EPN is deeply concerned that workers will not be protected under TSCA because of two policy decisions EPA has made. The first policy decision of concern is EPA's statement in the draft 1,4-Dioxane risk evaluation that the agency is "more likely to determine unreasonable risk exists for workers where risks greater than the acceptable benchmarks are identified for both central tendency and high end exposures under the conditions of use." Where risks greater than acceptable benchmarks are identified only for workers with high-end exposures, EPA will not make the determination that unreasonable risk occurs unless there are special circumstances. This policy is problematic because the agency is not factoring in worker exposure to contaminants in drinking water or other "regulated pathways" under central tendency or high-end conditions, so worker exposures are being underestimated under both scenarios. The second problematic policy is that when the agency finds unreasonable risk to workers, it dismisses that risk by assuming workers will use PPE the entire duration of the work activity throughout their careers, even when such equipment is not required, provided or used. This last point was demonstrated in the case of HBCD, which has no Occupational Safety and Health Administration or National Institution of Occupational Safety and Health standard, but EPA still overrode the risks to workers by assuming constant use of respirators and gloves.

In the 1,4-Dioxane draft risk evaluation, EPA stated that no consumer product exposures will be considered because its regulatory tools under TSCA Section 6(a) are better suited to addressing any unreasonable risks that might arise from these products through regulation of the activities that generate 1,4-Dioxane as an impurity or cause it to be present as a contaminant in the products. It is fine that EPA plans to prevent 1,4-Dioxane impurities in consumer products one day, but that does not eliminate the need to account for this pathway of exposure now as part of the cumulative exposure to the general population and workers.

EPN was also surprised to find that EPA spent considerable effort evaluating a threshold cancer risk model for 1,4-Dioxane when EPA's Office of Research and Development determined in 2013 that there was not sufficient evidence to support a mode of action (MOA) of cytotoxicity and regenerative cell proliferation. Given EPA's time constraints to deliver the first 10 chemical risk evaluations this year, it seems unwise to have spent time and resources to carry out an evaluation of this alternative cancer risk model, unless significant new information had been generated after 2013. EPN will be examining this issue in greater detail before submitting its second set of more detailed comments in August.

APPENDIX 3

Supplemental Comments on Draft Pigment Violet 29 Risk Evaluation

Under the Toxic Substance Control Act

July 10, 2019

The Environmental Protection Network (EPN) is an organization comprised of over 450 EPA alumni volunteering their time to protect the integrity of the U.S. Environmental Protection Agency (EPA), human health and the environment. We harness the expertise of former EPA career staff and confirmation-level appointees to provide an informed and rigorous defense against current administration efforts to undermine public health and environmental protections.

We make three points elaborated on below:

1. The current systematic review process has never been externally peer-reviewed.
2. The Pigment Violet 29 (PV29) database is inadequate and the approach to determine hazardous levels of exposure was computed with four uncertainty factors, missing a crucial fifth to account for database deficiencies.
3. EPA relied on inadequate data to reach the conclusion that PV29 does not present an unreasonable risk to health or the environment.

1. TSCA Systematic Review

On August 16, 2018, the EPN submitted comments (see Appendix 1) on EPA's draft guidance on a new systematic review process that was developed specifically for use in chemical risk evaluations under the Toxic Substance Control Act (TSCA); this process had never been externally peer-reviewed. In our comments, EPN advised against the use of this highly flawed draft methodology, as did numerous other organizations and experts in systematic review, as it departed substantially from accepted scientific principles for systematic review supported by the National Academy of Science's (NAS) Institute of Medicine and adopted by the National Toxicology Program. EPN commented that the draft TSCA process inexplicably did not build upon the years of progress in developing EPA's systematic review process for the Integrated Risk Information System (IRIS) program, which has been endorsed by the NAS. Our comments documented three critical flaws in the TSCA approach: 1) failure to include protocols to synthesize evidence from all the selected studies into a judgment about the weight of evidence as a whole; 2) use of an arbitrary quantitative scoring system for assessing and selecting individual studies; and 3) failure to adopt adequate implementation procedures for conducting the systematic review. EPN believes that these three critical flaws will lead the agency to exclude quality research and to select potentially biased studies for use, in direct opposition to the intent of conducting a systematic review in the first place.

Despite the well-documented flaws in this proposed systematic review process, EPA has not yet subjected the methods to peer review, but EPA has continued using the deficient TSCA review process for the TSCA risk evaluations of the first 10 chemicals and for the Safe Drinking Water Act risk assessment of GenX. At the June 20, 2019 meeting of the TSCA Science Advisory Committee on Chemicals (SACC), an EPA staff presentation indicated that over the next year SACC and the NAS would review the process, but verbal

discussion at the meeting clarified that there would not be a formal NAS review. The EPA staff presentation also documented that the TSCA systematic review process would not be revised to include the protocols on how to synthesize evidence from all the selected studies in order to make a determination of unreasonable risk. Instead EPA would address synthesis of studies on a chemical-by-chemical basis and would document the process used in each chemical risk evaluation.

EPN is commenting today on the April 2019 Pigment Violet 29 Systematic Review: Supplemental File for the TSCA Risk Evaluation. This supplemental file documents the changes that EPA made in response to public comments on its original assessment of relevant studies. First, quantitative scores for assessing the quality of an individual study are arbitrary and not science-based; the Cochrane Collaboration and the National Academy of Sciences recommend against such scoring methods.

In the updated supplemental file document, EPA continues to pursue quantitative scoring, which is arbitrary, and the major changes in the scoring of studies support our contention that the TSCA systematic review process is flawed and capricious. Furthermore, the TSCA regulation requires that the systematic review method be applied consistently to each evidence stream, but the TSCA method does not provide clear criteria for rating studies, nor can they. This inconsistency can be seen as approximately one-third of all the ratings of individual study aspects were downgraded from EPA's initial evaluation. This change in ratings was particularly problematic for the acute inhalation toxicity studies since inhalation is expected to be the main exposure pathway for workers. In the PV29 risk evaluation, EPA found no unreasonable inhalation risk for workers based on only two acute inhalation toxicity studies and a personal communication from Sun Chemical that an approximate maximum workplace air concentration of 0.5 mg/m3 would be expected over a 12-hour shift. This finding was despite the fact that EPA was forced to downgrade both acute inhalation toxicity studies from medium to unacceptable in the second round of scoring when public comments pointed out that ECHA summaries labeled them "not reliable." In addition, two acute oral toxicity studies and two eye irritation studies were downgraded to medium, while two acute intraperitoneal studies were downgraded to low confidence. Thus, EPA's systematic review methods should not use numeric scoring and must be improved before a reliable risk evaluation conclusion can be drawn.

EPA told the SACC that each chemical risk evaluation would describe how the agency synthesized the evidence from all the selected studies, but in the PV29 risk evaluation EPA does not adequately describe a specific protocol used to conclude that the chemical does not pose an unreasonable risk. [Biases from financial conflicts of interest were not rated.] There was no discussion of how the agency qualitatively rated the confidence in the overall body of evidence for PV29.

In conclusion, EPN recommends that EPA abandon the flawed TSCA "systematic review." Instead, EPA should implement a systematic review method that is compatible with empirically based existing methods and aligns with the Institute of Medicine's definition of a systematic review, including but not limited to, using explicit and pre-specified scientific methods for every step of the review. EPA should consider methods demonstrated for use in environmental health, and which have been endorsed and utilized by the National Academy of Sciences, i.e., the National Toxicology's Office of Health Assessment

and Translation systematic review method, and the Navigation Guide Systematic Review Method, and the IRIS program. EPA's TSCA systematic review framework should be peer-reviewed by qualified external experts in the field.

2. Adequacy of the PV29 Database and the Missing Uncertainty Factor

Comments submitted by EPN (see Appendix 8) and other parties during earlier comment periods questioned whether the hazard and exposure information available on PV29 was adequate to allow EPA to "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment….." If there was any doubt about the inadequacy of the foundation for making a determination at the time of initial issuance of the November 2018 draft Risk Evaluation for public comment, the recent downgrading by EPA of several of the toxicity studies meant to describe the potential for human hazard, as documented in the Supplemental files presented to the TSCA SACC for consideration during their recent peer review of the draft Risk Evaluation, completely dispels any myth of adequacy. It's time for the agency to admit that the database for PV29 is too insubstantial to support a risk determination. If EPA wishes to do so in the future, issuance of testing orders to fill the critical data gaps is the only reasonable next step to take.

EPA could have saved a lot of time and effort if it had followed long-standing agency-wide guidance on determining the adequacy of a toxicity database when deriving a Reference Dose (RfD) or Reference Concentration (RfC). The principles in place for RfD and RfC derivation also apply when characterizing a Benchmark Margin-of-Exposure (MOE), as was the approach taken for PV29. Implementation of these principles at an early stage in the assessment process would have led to the conclusion that the database for assessment of human hazard was too sparse to allow for a finding to be made, and that either the assessment should be abandoned or suspended until such time as adequate data have been requested and analyzed.

As pointed out by Dr. Scarano in his presentation to the SACC on June 19, 2019, there are a number of Uncertainty Factors that may be appropriate for application to a data set when deriving an RfD, RfC or Benchmark MOE as an estimate of "acceptable" human exposure to a chemical substance. He cited the following:

UF_H–Intraspecies –human-to-human variability/uncertainty
UF_A–Interspecies -animal-to-human variability/uncertainty
UF_S–Subchronic to Chronic extrapolation
UF_L–LOAEL-to-NOAEL extrapolation

What he did not mention was a fifth category of Uncertainty Factor:

UF_D_Database deficiencies

Each of these, when applied, generally does not exceed 10X, and may be lower; 3X is common. Agency application of this guidance is predicated upon a determination that, for a chronic exposure situation, a minimum database on which to estimate a high confidence reference value/MOE based upon animal

studies would consist of chronic dog and rat studies, along with reproductive and developmental bioassays (Dourson et al 1992; Dourson, et al 1996, US EPA, 2002). As a matter of policy, the composite UF should not exceed 3000 (US EPA, 2002).

Looking once more at the PV29 Draft Risk Evaluation, EPA used a MOE approach to assess data describing only non-cancer hazards. As a reminder, the MOE is the ratio of the point of departure (POD) dose from a toxicity study divided by the estimated or measured human exposure dose. This MOE is compared to a benchmark MOE. If the MOE exceeds the benchmark MOE, this indicates that risks to human health are not expected. EPA determined the Benchmark MOE to be =100, incorporating only the interspecies (UF_A), intraspecies (UF_H) and LOAEL-to-NOAEL (UF_L) Uncertainty Factors. However, because they were assessing a longer-term occupational exposure scenario, they also should have included an Uncertainty Factor for Subchronic to Chronic extrapolation (UF_S), as the study from which they selected the POD was of limited duration. Finally, because the toxicity database is so poor, they should have included an Uncertainty Factor for Database deficiencies (UF_D). Thus, the composite Uncertainty Factor would have been (UF_A x UF_H x UF_L x UF_S x UF_D) or (10 x 10 x 1 x 10 x 10)=10000. But since the agency's policy is that no composite UF should exceed 3000, the Benchmark MOE, in this instance, should be 3000. While this might not change the conclusions about risk associated with inhalation exposures, it would alter the conclusions reached with regard to dermal exposures. A comparison of the MOE for inhalation with the benchmark MOE (14,933/3000) and the MOE for the worst-case dermal exposure with the benchmark MOE (361/3000) indicate that risks may not be identified for workers based on inhalation exposure but would identify risks based upon dermal exposure, as only the inhalation MOE was greater than the benchmark MOE of 3000.

3. Additional Testing Is Necessary Under TSCA

The data insufficiency finding under TSCA is

> there is insufficient information and experience upon which the effects of manufacture, distribution in commerce, processing, use, or disposal of such substance or mixture or of any combination of such activities on health or the environment can reasonably be determined or predicted.

The converse of the data inadequacy finding under TSCA is that data should be adequate for reasonable determination or prediction of the substance's effects. As noted above, EPA relied on inadequate data to reach the conclusion that PV29 does not present an unreasonable risk. In addition, TSCA requires that health and safety information cannot be claimed as Confidential Business Information and must be made available to the public. These studies for PV29 are not fully available to the public.

EPN recognizes, as does TSCA, that comprehensive testing for every effect for every chemical is not feasible. However, it is critical that, for those relatively few chemicals selected for TSCA risk evaluations, sufficient data is available to support science-based determinations of risk. For PV29, EPA has based its conclusion of "no unreasonable risk" on insufficiently supported claims of low exposure, low bioavailability, and low toxicity observed only in short term studies. The available information is suggestive of a hypothesis

of low risk, but it is woefully insufficient to establish it. As tiered testing is encouraged by TSCA, EPA should, at a minimum, seek to confirm or reject this hypothesis by requiring acute inhalation toxicity studies, workplace monitoring, basic pharmacokinetic (PK) data measuring levels of PV29 in blood and distribution in fat, solubility studies and a 90-day subchronic test as directed by PK results. If these studies demonstrate PV29's potential for exposure and provide evidence of toxicity, further higher-tier testing would be necessary to address a broader range of end-points.

In addition, EPA noted that PV29 was expected to partition to soil and sediment. It, therefore, has no basis to conclude that there is no unreasonable risk to the environment without biodegradation data and data on the toxicity to benthic organisms.

EPA should use its testing authority under TSCA section 4. The Lautenberg amendments gave EPA authority to require testing by rule, order, or consent agreement when data are needed to conduct a risk evaluation or even to establish the priority of a chemical for risk evaluation. These amendments were designed to ensure that EPA can obtain the data needed to assess the risk of chemicals in commerce. In other words, the amendments were tailor-made for just this kind of situation.

The risk evaluation of PV29 is critical because it will be precedent setting and should signal the agency's commitment to identifying and filling significant data-gaps before it makes determinations of unreasonable risk. We recognize that, from the standpoint of the extent of testing required, PV29 may be an exception in the first group of chemicals selected for risk evaluation since its production and exposure are more limited than many other chemicals in this group. For high production volume, high exposure chemicals included in these initial and future risk evaluations, EPA should have data addressing the full spectrum of effects (e.g., mutagenicity, cancer, chronic effects, reproductive and developmental effects) before it concludes that there is no unreasonable risk to human health. Similarly, the agency should have the full range of data on relevant environmental effects when a chemical is released to the environment in substantial amounts.

EPA needs to establish criteria to determine the minimum data set necessary to make a risk determination. Without such criteria, it will appear to be an arbitrary judgment call on each chemical.

References:

Dourson, ML; Knauf, LA; Swartout, JC. (1992) On reference dose (RfD) and its underlying toxicity database. Toxicol Ind Health 8:171–189.

Dourson, ML; Felter, SP; Robinson, D. (1996) Evolution of science-based uncertainty factors in noncancer risk assessment. Regul Toxicol Pharmacol 24:108–120.

U.S. EPA. 2002. Review of the Reference Dose and Reference Concentration Processes. Final Report December 2002 EPA/630/P-02/002F Washington, DC.

APPENDIX 4

EPN Comments for the Public Meeting of the Science Advisory Committee on Chemicals Regarding Draft 1-Bromopropane Risk Evaluations Under the TSCA

August 30, 2019

The Environmental Protection Network (EPN) is an organization comprised of over 450 U.S. Environmental Protection Agency (EPA) alumni volunteering their time to protect the integrity of the EPA, human health and the environment. We harness the expertise of former EPA career staff and confirmation-level appointees to provide an informed and rigorous defense against current Administration efforts to undermine public health and environmental protections.

EPN is submitting these general comments to the Science Advisory Committee on Chemicals (SACC) to aid in their review of the 1-Bromopropane (1-BP) draft risk evaluation during their scheduled September 10-12, 2019, meeting.

1-BP is a solvent used in degreasing, dry cleaning, spray adhesives, and aerosol solvents that has been linked to neurological illnesses and may cause cancer and reproductive disorders.

On August 12, 2019, EPA published a Federal Register notice announcing the availability of documents and dates for the peer review of the draft risk evaluation for 1-Bromopropane (1-BP). While the official comment period on this draft risk evaluation is open until October 11, 2019, any commenters who wish for their comments to be considered by the SACC during their public meeting must submit their comments by August 30, 2019. While comments submitted after the August 30, 2019, deadline will still be provided to the SACC, they will not be able to contribute to any public dialog. EPN may prepare more detailed comments on this draft risk evaluation by the October 11, 2019, deadline; we are concerned, however, that the SACC will have concluded their review before the public comment period closes.

Once again, the agency is implementing a schedule for review that is inconsistent with best management practices. As EPN stated in its July 19, 2019, and August 30, 2019, comments on the 1,4-Dioxane and HBCD draft risk evaluations (see Appendices 2 and 5), we continue to be concerned that this process deprives the SACC of scientific and policy input that would be valuable in informing its review of the two draft evaluations and, thus, greatly reduce the value of the public comment process. This reoccurance reinforces the view articulated by commenters that the current agency approach seems to value an arbitrary deadline for a decision over the integrity of the information going into the decision. Furthermore, the process appears to be a mechanism to discourage comments from the stakeholder community that wishes to see a standardized risk evaluation process followed.

EPN is focusing these initial comments on the most critical policy issues that affect not only 1-BP but all future chemical risk evaluations under the Toxic Substances Control Act (TSCA).

1. As it has before, the agency is not using the best available tools by continuing to use the non-peer reviewed, flawed draft guidance document entitled "Application of Systematic Review in TSCA Risk Evaluations" to identify, sort, select, and exclude studies and other information to be used in the risk evaluation and, then, to grade their quality and acceptability for inclusion in the assessment.

   As stated initially in comments submitted on August 16, 2018 (see Appendix 1), and on several occasions since, EPN and other scientific groups presented detailed criticisms of that draft systematic review process. Our comments documented EPA's failure to follow necessary internal and external peer-review procedures in developing this process, described serious flaws permeating the entire TSCA systematic review process, and noted critical flaws in evaluating individual studies for use in toxicity assessments (such as failure to assess for bias). This draft guidance remains inconsistent with best practices in systematic review and should not be used for any purpose until peer reviewed and revised in accordance with the feedback received.

2. As with all chemicals selected for review in the Existing Chemicals Risk Evaluation program, EPN is concerned about the adequacy of the toxicity database used to assess potential for human health hazard. We have previously articulated our views on what constitutes a minimum database with which to estimate a high-confidence POD/reference value/MOE based upon animal studies.

   The draft risk evaluation includes the assessment of risk to workers and occupational non-users (ONUs) from acute and chronic inhalation and dermal exposures. EPA also evaluated the risk to consumer populations from inhalation and dermal acute and chronic exposures. Lifestages from infants to adults were included in the draft evaluation, by comparing the estimated exposures to acute and chronic human health hazards. However, pregnant women and workers considering a family were not specifically analyzed.

   What, then, would constitute a database adequate for assessing hazard to these (sub)populations? Our answer is that, absent fulsome observations in humans, the following types of information are needed:

   a. Studies that would illuminate the potential for general systemic toxicity over an exposure duration commensurate with that of the actual exposure scenario or that could be extrapolated from shorter-term exposure studies accompanied by the application of an uncertainty factor representing that extrapolation (e.g., acute short-term or subchronic to chronic);
   b. For chronic exposures, studies that would adequately test for carcinogenic potential by the relevant route(s) of exposure or could be extrapolated to those routes of exposure;
   c. For acute and chronic exposures, at least one developmental toxicity study;
   d. For shorter-term and chronic exposures, a one- or two-generation reproductive toxicity study, and;
   e. If nervous system effects are observed in exposed humans or animals, a more systematic evaluation of neurotoxicity and developmental neurotoxicity, since the worker population

includes women of child-bearing age and the general population includes infants and young children.

3. EPN continues to be concerned about the agency's approach for determining unreasonable risk to workers. It underestimates that risk by assuming workers will use personal protective equipment (PPE) for the entire duration of the work activity throughout their careers, even when such equipment is not required, provided or used. EPA continues to discount the risks to workers by assuming constant use of respirators. (See the testimony of Adam Finkel, former Regional Administrator and Director of Health Standards at OSHA (see Appendix 6). We would argue that while EPA may assess and characterize worker risk with and without the use of PPE, it should make its unreasonable risk determination based upon the "no PPE" scenarios. This would re-focus attention on many occupational use scenarios following non-cancer acute inhalation exposures to workers and ONUs that often included a "with PPE" component. Most consumer use scenarios constituted an unacceptable acute inhalation risk. PPE was not considered an option in these situations. There also are a substantial number of occupational use scenarios in which the non-cancer chronic inhalation risks were unacceptable for the unprotected worker and ONU at high end exposure levels, with worker risk unacceptable at central tendency levels. Sometimes the worker risk remained unacceptable even with PPE.

   Most cancer risk estimates following chronic inhalation exposure without PPE (both central tendency and high end) in occupational scenarios were unacceptable while some scenarios assuming PPE resulted in acceptable risk. Lacking the guarantee of consistent use of respirators, EPA should focus its regulatory options on mitigating risk to the unprotected individual.

APPENDIX 5

EPN Additional Comments on 1,4-Dioxane and HBCD

August 30, 2019

The Environmental Protection Network (EPN) is an organization comprised of over 450 U.S. Environmental Protection Agency (EPA) alumni volunteering their time to protect the integrity of EPA, human health and the environment. We harness the expertise of former EPA career staff and confirmation-level appointees to provide an informed and rigorous defense against current Administration efforts to undermine public health and environmental protections.

On July 19, 2019, EPN submitted general comments (see Appendix 2) on the 1,4-Dioxane and Cyclic Aliphatic Bromide Cluster (HBCD) draft risk evaluations to the Science Advisory Committee on Chemicals (SACC) for their July 29-August 2 meeting. These comments were submitted with the intention of submitting additional, more in-depth comments before the close of the public comment period on August 30.

Before addressing the two risk evaluations, EPN would like to underscore its concern that the SACC meeting at which the risk evaluations were discussed was scheduled prior to the deadline for filing comments. This is a reversal of the way EPA normally does things, is an approach that seems to value an arbitrary deadline over solid decision-making, and appears to be a mechanism to discourage public comment. The amount of time to develop comments before the SACC meeting was extremely compressed,. and we understand that detailed comments submitted after the meeting cannot now be considered by the SACC because it has completed its deliberations. This will deprive the SACC of scientific and policy input that would be valuable in informing its review of the two draft evaluations and greatly reduce the value of the public comment process. In the future, EPN strongly recommends that EPA schedule SACC meetings on draft risk evaluations after the close of the comment period so the SACC has a full opportunity to consider the comments.

EPN is filing these additional comments to expand on some of our earlier concerns and address an important issue we did not address previously—the adequacy of human health toxicity databases for the 1,4-Dioxane and HBCD draft risk evaluations in determining Benchmark Margins of Exposure (MOE) and on making findings on the presence or absence of Unreasonable Risk.

It is becoming clear now with four of the first ten draft Toxic Substance Control Act (TSCA) risk evaluations having been issued for public comment and peer review by the SACC, that adequacy and robustness of the database supporting the characterization of potential human hazard are not critical components of the agency's decision-making process on whether or not a chemical poses an unreasonable risk under TSCA. This became glaringly obvious at the time of the SACC review of Pigment Violet 29 (PV29) in June 2019 when the agency abruptly disavowed and re-characterized as inadequate studies originally thought to be the best potential candidates to serve as the basis for

calculating Points of Departure (PODs) and determining the adequacy of Benchmark Margins of Exposure; together with serious limitations in the PV20 database, this reversal left the agency with little data of value on which to base this calculation and, subsequently, to make a risk finding.

EPN commented, in its second round of comments on PV29 (see Appendix 9), that the agency should have followed long-standing agency-wide consensus guidance on determining the adequacy of a toxicity database when deriving a Reference Dose (RfD) or Reference Concentration (RfC) and/or a POD and MOE. Dr. Stan Barone of EPA's Office of Chemical Safety and Pollution Prevention (OPPT) made a comment during the July 29-August 2 SACC meeting that it is not policy to consider database inadequacies/deficiencies when judging the adequacy of an MOE. If he was ascribing this to agency policy, he is flat out wrong. If he was ascribing it to OPPT, that office is out of compliance with agency-wide consensus guidance. The principles in place for RfD and RfC derivation also apply when characterizing an MOE. As stated in the 2002 EPA document Review of the Reference Dose and Reference Concentration Processes, "The methodology recommended in the RfD document is considered generally applicable to both cancer and noncancer endpoints where dose-response relationships are thought to be either nonlinear or consistent with a threshold. Although the emphasis in this document is on the calculation of RfDs and RfCs, **the same processes and considerations are applicable to the margin of exposure (MOE)** (emphasis added)**……"** (U.S. EPA, 2002, page 1-2).

The 1993 *Reference Dose (RfD): Description and Use in Health Risk Assessments Background Document 1A*) and Barnes and Dourson (1988) summarize the agency consensus guidelines on the use of Uncertainty and Modifying Factors in the derivation of an RfD (or an RfC or a POD or an MOE). At that time, there were four Uncertainty Factors (UF) and one Modifying Factor, which is now also called an Uncertainty Factor (UF_D for data deficiencies). This latter UF is an additional uncertainty factor that is greater than zero and less than or equal to 10. The default value for this UF is one. The magnitude of the UF depends upon the professional assessment of scientific uncertainties in the key study(ies) and the database not explicitly covered by the other four UFs ($UF_{H,}$ Intraspecies-human-to-human variability/uncertainty; $UF_{A,}$ Interspecies-animal-to-human variability/uncertainty; $UF_{S,}$ Subchronic-to-Chronic extrapolation; $UF_{L,}$ LOAEL-to-NOAEL extrapolation). Importantly, it addresses the completeness of the overall database.

EPN noted in its second round of comments on PV29 (see Appendix 9) that agency application of this guidance is predicated upon a determination that, for a chronic exposure scenario, a minimum database on which to estimate a high-confidence POD/reference value/MOE based upon animal studies would consist of chronic dog and rat studies, along with reproductive and developmental bioassays (Dourson et al., 1992; Dourson et al., 1996; U.S. EPA, 2002). As a matter of policy, the composite UF should not exceed 3,000 (U.S. EPA, 2002). Some modification of these requirements may be in order as the regulatory community in the U.S. (i.e., EPA and FDA) and elsewhere has concluded that the chronic dog study is of little added value and can be phased out as a regulatory requirement, and that a subchronic study provides adequate information in this species (e.g., Dellarco et al, 2010). However, it could be argued that, in certain circumstances, additional information on other endpoints of concern would

warrant inclusion in the minimal data set to best understand an agent's hazard potential. These endpoints could include immunotoxicity or neurotoxicity.

TSCA Existing Chemical risk evaluations and their associated risk management decisions essentially represent a lifetime regulatory statement given that there are many thousands of commodity chemicals to prioritize and assess (or not) and given that there is no requirement on the part of the agency to revisit these assessments and decisions at any time (unlike the pesticide regulatory program). Therefore, the agency has an obligation to get it right the first time it conducts a risk evaluation because, essentially, it's the only time it will address the health and environmental effects of a chemical of concern. Judging the completeness and integrity of individual studies and databases and properly selecting PODs/RfDs/RfCs and Benchmark MOEs are key elements of that obligation.

The 2016 Frank R. Lautenberg Chemical Safety for the 21st Century Act (the "new" TSCA) eased the conditions under Section 4 of the Act whereby the agency can issue orders/regulations and enter into consent agreements requiring manufacturers (including importers) or processors to test chemical substances and mixtures. TSCA authorizes this testing ito develop data about health, environmental effects and/or exposure when there are insufficient data to determine whether a chemical substance or mixture presents an unreasonable risk to human health or the environment. The law specifically enables EPA to require testing where necessary for a risk evaluation.

One would expect that the agency would take full advantage of this new authority and conduct a testing/research needs assessment in concert with its prioritization and evaluation programs so that any filling of data gaps would be completed BEFORE a Risk Determination is attempted. To date, there is no evidence of any EPA requests for generation of additional data under TSCA section 4 despite the significant data-gaps on several of the chemicals on which risk evaluations are being conducted. Incorporation of a UF in the calculation of PODs/RfDs/RfCs and/or MOEs should be considered a stopgap measure and not the final solution for data inadequacies.

So what, then, should the UF for data deficiencies be for 1,4-Dioxane and HBCD? And, how would it affect the conclusions concerning unreasonable risk for the various scenarios assessed for these two chemicals?

<u>1,4-Dioxane</u>

1,4-Dioxane is an impurity in a broad range of personal care and cleaning products used by millions of consumers. These "down the drain" products also contribute 1,4-Dioxane to wastewater and surface water and, together with other sources of contamination, account for the widespread presence of 1,4-Dioxane in drinking water. Drinking water contaminated with 1,4-Dioxane has been detected in numerous regions of the US and has prompted significant health concerns in several states and local communities. EPA unjustifiably failed to address these significant sources of exposure and risk to the general population. Had it done so, it presumably would have calculated MOEs for relevant exposure

scenarios and, in so doing, applied UFs that reflected inadequacies in the available health effects data for 1,4-Dioxane.

The agency focused its assessment only on worker acute/short-term and chronic dermal and inhalation exposure scenarios in a variety of manufacture, use and disposal settings. Workers were divided into two categories: users and occupational non-users (ONUs). The workers were assumed to be healthy males and females, at least 16 years of age. Both non-cancer and cancer endpoints were assessed and quantified.

What, then, would constitute a database adequate for assessing hazard to this demographic? Our answer is that, absent observations in humans, the following types of information are needed:

1. Studies that would illuminate the potential for general systemic toxicity over an exposure duration commensurate with that of the actual exposure scenario or that could be extrapolated from shorter-term exposure studies accompanied by the application of an uncertainty factor representing that extrapolation (e.g., acute short-term or subchronic to chronic);
2. For chronic exposures, studies that would adequately test for carcinogenic potential by the relevant route(s) of exposure or could be extrapolated to those routes of exposure;
3. For acute, shorter-term and chronic exposures, at least one developmental toxicity study;
4. For shorter-term and chronic exposures, a one- or two-generation reproductive toxicity study, and;
5. If central nervous system effects are observed in acutely exposed humans and animals, a more systematic evaluation of neurotoxicity and developmental neurotoxicity, since the worker population includes women of child-bearing age.

The database for 1,4-Dioxane meets the criteria for Items #1-3, but is lacking in Items #4 and #5. These are substantial data gaps, warranting an additional UF of tenfold for data deficiencies when determining the Benchmark MOE for both exposure durations and routes. Thus, the Benchmark MOE for acute/short-term inhalation risks should be increased from 300 to 3,000, and the chronic inhalation and dermal Benchmark MOEs from 30 to 300.

Using this revised Benchmark MOE for the acute/short-term inhalation scenarios, there is a shift to unreasonable risk for the following:

1. Manufacturing, Lab Chemicals and Dry Film Lubricant—central tendency, without personal protective equipment (PPE), and high end with respirator;
2. Import/Repackaging (Bottle), Import/Repackaging (Bottle), Industrial Use, and Disposal—both central tendency and high end with respirator;
3. Film Cement—high end with respirator, and;
4. Use of Printing Inks (3D)—central tendency and high end, without PPE.

For the chronic inhalation scenarios, a shift to unreasonable risk would result for the following:

1. Spray Application—both central tendency and high end, without PPE;
2. Manufacturing, Import/Packaging, Lab Chemicals and Disposal—central tendency with respirator, and;

3. Film Cement, Use of Printing Inks (3D) and Dry Film Lubricant—central tendency and high end with respirator.

For the chronic dermal scenarios, a shift to unreasonable risk would result only for film cement—central tendency and high end with respirator.

It should be noted that for most of the worker exposure scenarios EPA addressed in the draft evaluation, it concluded that risks were not unreasonable assuming effective and continuous use of Personal Protective Equipment (PPE) by exposed workers. As EPN has previously maintained, this assumption is not supportable. For 1,4-Dioxane, there are no OSHA standards that require use of PPE and EPA presents no empirical evidence that PPE is widely and effectively used during manufacture and processing of 1,4-Dioxane. Without assuming the use of PPE, most of EPA's calculated MOEs are smaller than than the benchmark and demonstrate unreasonable risks to workers. The above analysis demonstrates that if a proper UF is applied to account for data-base uncertainty, even the MOEs for some PPE scenarios are smaller than the benchmark and thus demonstrate unreasonable risks. This indicates that EPA should be making unreasonable risk determinations for the great majority of exposed workers.

In its June 19 comments, EPN noted that it would follow-up with additional comments with regard to the degree of evidence available to support the characterization of potential mode(s) of action (MOA) by which the liver tumors observed in the rodent bioassays were produced. Both the 2013 IRIS assessment and the OPPT draft Risk Evaluation conclude that the available data are sufficient to rule out a mutagenic mode of action, but they are not sufficient to support a non-linear MOA characterized by cytotoxicity and regenerative hyperplasia. While some of the data appeared to be indicative of such an MOA, they did not all fit properly into the right places, sequence and temporality. Furthermore, there remain some critical data gaps. In addition, there was inadequate information on the MOAs for all the other tumor types observed in multiple animal studies. Thus, we came to the same conclusions as articulated in the IRIS and OPPT documents on data adequacy, and agree that the default linear approach for quantitative assessment remains the appropriate option.

<u>HBCD</u>

In its assessment of HBCD, the agency considered potential exposures resulting from consumer activities and uses, industrial and commercial activities, and environmental releases and wastes. It considered workers and ONUs, which include men and women of reproductive age. Consumer exposure was assessed for various pathways for all age groups, including adults and children. Non-users could be any age group ranging from infants to adults. Also, it considered exposures to the general population for all age groups, as well as additional considerations for other exposed groups.

A variety of acute and chronic exposure scenarios was assessed. Only non-cancer effects were assessed and quantified, as no adequate cancer bioassays have been conducted with HBCD.

Populations of interest and exposure scenarios included the following:

- Workers: Acute-Adult worker (>21 years old) and female workers of reproductive age (>16 year to less than 50 years old) exposed to HBCD for a single 8-hr exposure;
- Chronic-Adult worker: (>21 years old) and female workers of reproductive age (>16 year to less than 50 years old) exposed to HBCD for the entire 8-hr workday for 260 days per year for 40 working years;
- ONU: Acute or Chronic-Adult worker (>21 years old) and female workers of reproductive age (>16 year to less than 50 years old) exposed to HBCD indirectly by being in the same work area of the building;
- General Population (Background Exposure): Acute or Chronic-Infant, Young Toddler, Toddler, Small Child, Child, Teen, Adult, and;
- Highly Exposed Population (NearFacility): Acute or Chronic-Infant, Young Toddler, Toddler, Small Child, Child, Teen, Adult.

What, then, would constitute a database adequate for assessing hazard for these demographics? Our answer is that, absent relevant observations in humans, it would include the following studies:

1. Studies that would illuminate the potential for general systemic toxicity over exposure durations commensurate with those of the actual exposure scenario(s) or that could be extrapolated from shorter-term exposure studies accompanied by the application of an uncertainty factor that represented that extrapolation (e.g., subchronic to chronic);
2. For chronic exposures, studies that would adequately test for carcinogenic potential, particularly given HBCD's potential for persistence and bioaccumulation;
3. For acute and chronic exposures, at least one developmental toxicity study;
4. For chronic exposures, a one- or two-generation reproductive toxicity study in rodents, and;
5. Given inconclusive evidence of thyroid effects in humans but confirmed dose-related effects in animals observed across multiple rat strains, sexes, exposure durations, and study designs, a systematic evaluation of developmental neurotoxicity, as the worker population includes women of child-bearing age, and the general population includes infants and young children.

The database for HBCD meets the criteria for Items #1 and #3-5, but not Item #2 (testing for carcinogenic potential). Given HBCD's polybutylene terephthalate characteristics, this is an important data gap, warranting an additional UF of threefold for data deficiencies when determining the Benchmark MOE for both acute and chronic exposure durations, and for all routes, and for all of the (sub)populations included in the risk evaluation. Thus, the Benchmark MOEs for all exposure scenarios (endpoints, routes and populations) should be increased at least threefold, although one could argue for a tenfold UF as well.

The consequences of this change are plenty, primarily in the occupational sector, assuming an additional UF of threefold.

- **Fourteen (14)** scenarios shift to Unreasonable Risk in the Risk Estimation for Non-Cancer Effects Following Acute Inhalation Exposures, Occupational Scenarios (Table 4-9).
- **Twenty-five (25)** scenarios shift to Unreasonable Risk in the Risk Estimation for Non-Cancer Effects Following Chronic Inhalation Exposures, Occupational Scenarios (Table 4-10).
- **No (0)** scenarios shift to Unreasonable Risk in the Risk Estimation for Non-Cancer Effects Following Acute Dermal Exposures (Table 4-11).
- **Eleven (11)** scenarios shift to Unreasonable Risk in the Risk Estimation for Workers Non-Cancer Effects Following Chronic Dermal Exposures in Occupational Scenarios (Table 4-12).
- **No (0)** scenarios shift to Unreasonable Risk in the Risk Estimation for Non-Cancer Effects – General Population Table 4-13.
- **Four (4)** scenarios shift to Unreasonable Risk in the Risk Estimation for Non-Cancer Effects Following Acute Exposure to Highly Exposed Population (Table 4-14).
- **No (0)** scenarios shift to Unreasonable Risk in the Risk Estimate for Non-Cancer Effects Following Acute Exposure to Highly Exposed Population – Inhalation (Table 4-15).
- **No (0)** scenarios shift to Unreasonable Risk in the Risk Estimate for Non-Cancer Effects Following Acute Exposure to Highly Exposed Populations—Consumer Articles (Table 4-16).
- **Seven (7)** scenarios shift to Unreasonable Risk in the Risk Estimate for Non-Cancer Effects Following Chronic Exposure to Highly Exposed Population (Table 4-17).
- **No (0)** scenarios shift to Unreasonable Risk in the Risk Estimate for Non-Cancer Effects Following Chronic Exposure to Highly Exposed Populations—Consumer Articles (Table 4-18).

Consideration of database adequacy and application of the UF_D when it is not adequate is consequential for the risk evaluations of both 1,4-Dioxane and HBCD. EPA should clearly reconsider its risk evaluations and exercise its "new" TSCA section 4 mandate.

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APPENDIX 6

U.S. EPA, Office of Pollution Prevention and Toxics
Electronically Submitted via Regulations.gov

Re: Docket ID No. EPA-HQ-OPPT-2019-0235
TSCA Science Advisory Committee on Chemicals Meeting to Evaluate 1-Bromopropane

August 30, 2019

Dear Sirs:

I offer the following comments to the TSCA Science Advisory Committee on Chemicals (SACC) in advance of its September 10-12 meeting to discuss the EPA Draft Risk Evaluation for 1-Bromopropane (hereafter "Draft"). EPA released this 406-page document, along with numerous supplemental files, only 2 ½ weeks ago, with a deadline of today to provide pre-meeting comments to the SACC. Accordingly, I am confining these comments to four overarching concerns I have about the Draft.

I have summarized my work on 1-BP in several prior sets of comments to EPA, primarily to OAQPS as it continues its inexplicable and nearly 10-year-long failure to acknowledge the obvious facts that 1-BP is a known rodent carcinogen and a known human and animal neurotoxin, and that it therefore must by law be listed as a Hazardous Air Pollutant (HAP). Suffice it to say here that I nominated 1-BP for its eventual testing by the National Toxicology Program in 1999, when I was OSHA's Director of Health Standards, and later helped the city of Philadelphia promulgate an ordinance in 2010 setting a 40 ppb exposure limit for 1-BP in commercial and residential spaces adjacent to dry cleaners.

I urge the SACC to seriously consider whether the Draft can be released until these four deficiencies are corrected:

1. EPA's "Virtually Safe" Exposure Level for Neurotoxicity is roughly 10x Higher than a Level Already Found to be Unsafe in Humans.

The most sensitive endpoint EPA has chosen for the POD for chronic, non-carcinogenic effects of 1-BP, is 18.2 ppm (HEC=25 ppm), as seen on p. 173 of the Draft. This comes from studies of rats. But reasonable human data are generally preferred to rodent data, and here we have multiple studies showing human neurological effects far below 25 ppm. EPA acknowledges this (p. 157), noting that at least three worker studies showed adverse effects on nerve conduction at TWA levels around 1 to 4 ppm.

In Appendix I.4, EPA makes various attempts to invalidate these studies, but I find the arguments scattershot and unconvincing. In particular, EPA invokes exposure misclassification without much foundation, and fails to mention that this would generally bias a study away from a significant positive finding. In addition, EPA fails to cite a second study by Li et al. in 2010 (see reference list at the end of these comments).

I urge the SACC to review Appendix I.4 and consider why EPA is relying on a 25 ppm POD from rodent data in the face of multiple studies showing a human LOAEL much lower than that. All of the MOE estimates for neurotoxicity are biased high on account of this inexplicable decision by EPA; in other words, the non-cancer risks EPA concluded were unacceptable are "more unacceptable" than EPA admits, and some of the "acceptable" scenarios may not be acceptable at all.

2. EPA May Underestimate the Central Tendency and Reasonable Worst-Case Worker Exposures.

In previous comments, I urged EPA to make use of the extensive "SLCTC" (Salt Lake City Technical Center) database OSHA maintains on worker exposures (previous EPA documents on 1-BP had only used the much smaller "IMIS" dataset), and I appreciate EPA's efforts to obtain and analyze these data. I am concerned, however, that EPA's overall appraisal of worker exposures (see esp. Table 2-39) underestimates the extent of exposures to 1-BP. I have analyzed 304 air samples (available online via search at https://www.osha.gov/opengov/healthsamples.html, using "IMIS code" R290) OSHA took for 1-BP between 1998 and 2018, and found that the mean concentration across all industry sectors was approximately 29 ppm, with a 95th percentile value of 170 ppm. Both of these values, of course, are (far) above the HEC of 25 ppm EPA derived from rodent studies, for an MOE of (far) less than 1, when (see below) EPA considers an MOE less than 100 to be unacceptable.

EPA acknowledges in the Draft that in many occupational scenarios, the MOEs are unacceptably low. Nevertheless, in only 2 of the 20 worker scenarios (not counting the "post-EC" scenarios, for reasons given below) are the central-tendency estimates of exposure greater than the overall mean of 20 ppm (sprayers and non-sprayers in adhesives use)—so I am concerned that EPA has somehow underestimated the mean and high-end exposures in many of the other 18 scenarios, where estimated median exposures (according to EPA) generally are less than 1 ppm. It is hard to understand how the overall measured mean exposure could be 29 ppm when so few of the separate scenarios have medians above 10 ppm.

In addition, EPA should be using means (arithmetic averages), not medians, to characterize the central tendency of exposure. In non-negative distributions, the median

underestimates the mean. In the 304 samples I analyzed, the mean:median ratio was approximately 6:1, so using the mean would yield much higher risk estimates (much lower MOEs).

Also, EPA should not construct "post engineering controls" scenarios to hypothesize what exposures to 1-BP might be if, contrary to fact, there are any OSHA or EPA requirements to actually install engineering controls.

3.EPA has no Basis for Assuming that Workers will Wear Respirators, that the Generous "Assigned Protection Factors" Will be Achieved, or that the Cartridges Will Provide Adequate Protection against 1-BP.

First, it is simply inappropriate, in the absence of any required OSHA controls on 1-BP, to assume that employers will provide respirators to their workers. On page 57, EPA cites OSHA's Respiratory Protection Standard (29 CFR 1910.134), but that standard only requires respirator use when ambient workplace concentrations exceed an OSHA PEL (Permissible Exposure Limit, PEL), and there is no OSHA PEL for 1-BP nor (in my intimate knowledge of that agency) is there likely to be one in the foreseeable future—not because 1-BP is not a serious workplace hazard, but for other reasons. The SACC should encourage EPA to cease the practice of diluting risk estimates based on unwarranted assumptions about respirator use.

But even if respirators are used in some exemplary workplaces using 1-BP, EPA is using an overly optimistic set of Assigned Protection Factors (APFs), with the effect of making worker exposure seem less than it will be if respirators are worn. I urge EPA to work with OSHA to evaluate the more precautionary (and in my expert opinion, more scientifically valid) set of APFs we developed circa 1999-2002, before OSHA decided to change the APFs to make them less protective. We used a sophisticated Markov Chain Monte Carlo process to parse available data on outside- to inside-mask concentration ratios, in order to separately evaluate within-worker versus between-worker variability in the adequacy of face-seal fit of each respirator make and model. This analysis, for example, strongly suggested that the correct (reasonable worst-case) APF for a half-mask was 5, not the value of 10 that OSHA subsequently adopted.

And even more concerning is EPA's complete inattention to the other, and more significant, component of respirator non-protection: the breakthrough of organic solvents like 1-BP through the carbon or other medium in organic vapor cartridges. A word-search of the entire EPA Draft revealed only three instances of the word "cartridge" (none having anything to do with their (in)adequacy), and no instances of the word "breakthrough." I am unsure of whether any published study has evaluated how long it takes for a typical concentration of 1-BP to migrate through an organic-vapor cartridge and thereupon expose

the user to much higher concentrations than while the cartridge was providing protection.

Surely EPA should not implicitly assume, as it does here, that OV cartridges are 100% effective for the entire work shift (or longer if employers are unaware that cartridges must have empirically-derived "change schedules," and end up supplying workers with the same cartridge day after day!). But there are a few published studies estimating breakthrough time based on physical parameters of the agent such as boiling point or molecular weight. See the Tanaka et al (1999) references below: these investigators found that a simple linear regression of boiling point versus breakthrough time gave good predictions. Using 1-BPs boiling point of 71 °C (and using the reference compound (cyclohexane) breakthrough time of 124 minutes), this equation would predict 1-BP breakthrough within about 117 minutes. In other words, the complete protection EPA assumes an OV cartridge would provide would begin to go to zero within 2 hours of every workshift, unless employers were knowledgeable and willing to provide 4 cartridges to each worker during every 8-hour workday…

4.EPA Has no Basis to Claim that the 2011 (!?) Petitions to List 1-BP as a HAP are Germane to this Risk Assessment Exercise.

EPA's claim (p. 27 of the Draft) that "the listing of 1-BP as a Hazardous Air Pollutant (HAP) will address the inhalation exposure pathway via ambient air to the general population, which eliminated the need for evaluation," makes no sense. The process for adding a substance to the HAPs list is entirely a hazard-identification one: the Clean Air Act Amendments of 1990 make clear that an air pollutant "shall" be added if it is "known to cause or may reasonably be anticipated to cause adverse effects to human health or adverse environmental effects." No risk assessment is required to make this decision, and so the "evaluation" EPA is punting on here will not be conducted as part of the consideration of the petitions filed in 2011 by industry and the New York state agency. This straightforward hazard-identification exercise, for a known neurotoxin and rodent carcinogen, has been stalled at EPA for nearly eight years. So, the claim that if at long last 1-BP is formally declared to be neurotoxic and carcinogenic, the general population will somehow be protected, seems both illogical and cynical given the pace of EPA's activity here.

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In addition to these scientific comments, I offer one suggestion about the exposition of virtually the entire risk characterization sections for non-carcinogenic effects. There seems to be a gradual evolution of the meaning of "Margin of Exposure" (MOE) at EPA. Initially, EPA construed the MOE as the factor by which the maximum desired level of exposure exceeds the actual exposure. With this usage, it was always clear that an MOE

less than 1.0 was clearly unacceptable (actual exposure being greater than "safe" exposure; denominator exceeding numerator). But now, EPA is changing the numerator of the MOE fraction from (a) a level acceptable for residents, consumers, or workers to (b) a level N orders of magnitude above the acceptable level. With this change, now the MOE has to be less than 10N to be acceptable (and in this document, N=2, so the MOE just has to be less than 100.

This change-of-scale is coherent as far as it goes, but I worry that readers of EPA documents may misunderstand—or be manipulated by others into misunderstanding—what is really going on. The "new" numerator of the MOE is clearly not a safe level—it is a level known or modeled to correspond to some non-zero level of harm, one that has not undergone any of the various "adjustment factors" that might bring it down to a level "likely to be without appreciable risk of harm." OK—but then it becomes crucial for EPA and downstream commenters to always highlight the fact that the desired 10N multiple of the (BMDL/exposure) must be attained. It would be unacceptable for anyone to claim that "the MOE is less than (say) 100 here, but it's still a large number."

The "old" way, no one could get away with saying an MOE < 1 is not clearly unacceptable; the "new" way, a hypothetical MOE of 90 is not "almost 100"—it is a case of unacceptably high exposure. In other words, the use of "the MOE needs to be at least 100" can easily lead to statements like "we've provided a margin of safety of 90, which is almost as good as 100." No—there is no safety at all below 100x, just as the old way there was no safety at all below 1x. I hope the SACC will encourage EPA to rethink this confusing and circuitous exposition method.

Thank you for the opportunity to comment on this important matter.

Sincerely,

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[formerly OSHA's Director of Health Standards and Regional Administrator (VIII)]
(affiliations listed for purposes of identification only)

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APPENDIX 7
COMMENTS
EPA Problem Formulations for Asbestos, HBCD and Carbon Tetrachloride
July 26, 2018

Introduction

The Environmental Protection Network (EPN) is providing the following comments on the problem formulations for asbestos, HBCD and carbon tetrachloride, which we find are setting improper precedents for future chemical risk evaluations under the new Chemical Safety Act amendment to TSCA. The final rule states that EPA is given discretion to determine the conditions of use that it will address in its evaluation of a priority chemical, "in order to ensure the agency's focus is on the conditions of use that raise the greatest potential for risk." The final rule mentions excluding de minimis conditions of use or conditions of use that have been adequately addressed by another regulatory agency. The final rule also states that while the statute is ambiguous as to whether the conditions of use should include legacy uses, "in a particular risk evaluation, EPA may consider background exposures from legacy use, associated disposal and legacy disposal as part of an assessment of aggregate exposure or as a tool to evaluate the risk of exposures resulting from non-legacy uses."

In contrast to this final rule, the Chemical Safety Act is clear that EPA must identify and evaluate risks resulting from all intended or reasonably foreseen, as well as known conditions of use of a chemical substance. EPA is required to make a determination on the chemical substance as to whether it presents an unreasonable risk of injury to health or the environment without consideration of costs or other non-risk factors due to a single use or any combination of uses. If an unreasonable risk is found, TSCA provides EPA with a broad set of authorities to deploy actions that fully eliminate the unreasonable risk. The timing, frequency, location and duration of all exposures and their magnitude at a given point in time and space are key to determining unreasonable risk for susceptible subpopulations such as infants, pregnant women, the elderly, workers and disproportionately exposed communities. TSCA requires two kinds of risk assessment, one for a single or sentinel exposure to evaluate acute toxic effects and one for aggregate exposure of co-occurring sources to evaluate chronic toxic effects. Since all 10 chemicals addressed in these first problem formulations have chronic toxic effects, a comprehensive aggregate assessment of all co-occurring exposures is critical since excluding even one pathway will underestimate cancer and non-cancer effects.

In the following sections of our public comments, the Environmental Protection Network will explain: 1) why the asbestos and HBCD problem formulations should not exclude pathways of exposure to legacy uses; 2) why the asbestos problem formulation should not exclude pathways of exposure regulated under other programs; 3) why the carbon tetrachloride problem formulation should either evaluate the conditions of use now designated as "de minimis" or provide a science-based justification for their exclusion and rationale for not seeking additional information from industry; and 4) why EPA needs to take the lead in addressing workplace risks while consulting with OSHA.

1. <u>EPA's Proposed Approach to Risk Evaluation of Exposures Related to Legacy Use Is Flawed</u>

The exclusion of "legacy" exposures in the problem formulation documents is particularly flawed for asbestos, and very likely problematic for the cyclic aliphatic bromide cluster chemicals (HBCD) as well.

While much of the current risks from asbestos occur among workers involved in asbestos abatement or removal during remodeling, demolition and disposal, there are also risks among maintenance workers with in-place asbestos and auto mechanics performing brake work. Reports published by CDC and IARC strongly suggest that these uses contribute to the widespread release of fibers into the general environment, even with adherence to OSHA and other regulatory limits.

It is well documented that asbestos is a carcinogenic compound. There is no safe level of exposure. The ATSDR noted that asbestos is a dangerous substance and should be avoided. Risk is dependent on frequency and duration of exposure. Breathing asbestos can cause asbestosis, lung cancer and mesothelioma. This was the finding reported in the EPA peer-reviewed report on the destruction of the World Trade Center.[11] This report stated that the continuing release of asbestos fibers posed a serious hazard to humans unknowingly exposed to residual fibers and would continue to do so for a long period of time. Exposure risks were also addressed in an EPA 2004 pamphlet describing risks from release of asbestos fibers from brake pads.[12] In the pamphlet, EPA stated that asbestos exposures during daily work on brakes and during the disposal of asbestos-containing products are a serious concern for the mechanics and other workers within the facility.

In addition, asbestos is described in the problem formulation document as primarily a respiratory disease hazard (asbestosis, lung cancer and mesothelioma), but there is strong evidence to suggest that asbestos also poses a risk of stomach, larynx, pharynx and possibly reproductive system cancers. These risks are dismissed in the problem formulation document without explanation. They should be part of the comprehensive risk assessment.

Knowing that everyone is exposed to some level of background asbestos exposure is not a reason to ignore the hazards that remain from legacy exposures such as the removal of in-place asbestos materials, and the exposure of populations who live near former mines that have produced contaminated living environments. It would be a reckless decision to ignore the long-term exposures that still occur from legacy pathways and their resultant health hazards. A recent example of asbestos exposure occurred in Manhattan when a steam pipe lined with asbestos exploded on July 19, 2018 (*New York Times*, July 19, 2018).

A similar situation likely exists with regard to HBCD. While these chemicals are reportedly no longer manufactured in the U.S., they are still imported and used. There is very likely a substantial amount of legacy materials in place arising from past use in building insulation. Safer Chemicals, Healthy Families estimates that most of the 30,000 to 60,000 metric tons of HBCD used in the U.S. between 1988 and 2010 was used in building insulation and that much of it "will reach the end of its useful life in the years ahead."[13] The potential exposure resulting from the removal of the legacy insulation through demolition, remodeling and

[11] EPA Report: Selecting Contaminants of Potential Concern and Setting Health-Based Benchmarks, May 2003, Prepared by the Contaminants of Potential Concern (COPC) Committee of the World Trade Center Indoor Air Task Force Working Group.
[12] EPA-747-04-004
[13] EPA Docket ID Number EPA-HQ-OPPT-2016-0735

disposal, as is the case with asbestos containing materials, may pose risks, and there are no OSHA standards to protect the workers involved in such activities. Therefore, the legacy activities involving HBCD-containing materials must be evaluated if EPA is to successfully fulfill its responsibilities to comprehensively assess and eventually manage the exposures and risks of HBCD under TSCA.

2. EPA's Proposed Approach to Risk Evaluation of Exposures Associated with Other EPA Regulatory Programs is Contrary to Plain Statutory Language and is Legally Unsound; is Scientifically and Methodologically Unsound and is Not Efficient.

Overview

In each of the draft problem formulation documents for the first ten existing chemicals, EPA includes the following paragraphs (see, for example, page 13 of the 1-Bromopropane Problem Formulation):

> ". . . EPA also identified certain exposure pathways that are under the jurisdiction of regulatory programs and associated analytical processes carried out under other EPA-administered environmental statutes – namely, the Safe Drinking Water Act (SDWA), the Clean Water Act (CWA), and the Resource Conservation and Recovery Act (RCRA) – and which EPA does not expect to include in the risk evaluation.
>
> As a general matter, EPA believes that certain programs under other Federal environmental laws adequately assess and effectively manage the risks for the covered exposure pathways. To use Agency resources efficiently under the TSCA program, to avoid duplicating efforts taken pursuant to other Agency programs, to maximize scientific and analytical efforts, and to meet the three-year statutory deadline, EPA is planning to exercise its discretion under TSCA 6(b)(4)(D) to focus its analytical efforts on exposures that are likely to present the greatest concern and consequently merit a risk evaluation under TSCA, by excluding, on a case-by-case basis, certain exposure pathways that fall under the jurisdiction of other EPA-administered statutes. EPA does not expect to include any such excluded pathways as further explained below in the risk evaluation. The provisions of various EPA-administered environmental statutes and their implementing regulations represent the judgment of Congress and the Administrator, respectively, as to the degree of health and environmental risk reduction that is sufficient under the various environmental statutes."

Although these paragraphs are contained in all ten of the problem formulation documents, EPA offers no further definition of what it means by "under the jurisdiction" of regulatory programs or, "associated analytical processes . . .under other EPA administered statutes." We have focused our comments on this issue in the asbestos problem formulation as an example case. All of our objections and concerns about this approach for asbestos would apply to the other nine chemicals, and depending on specifics, the use of this approach for those chemicals would likely raise additional concerns as well.

Comments on Exclusion of Consideration of Exposures Associated with Other EPA Regulatory Programs, with specific reference to the asbestos problem formulation:

a. EPA's planned approach to exclude exposure pathways associated with other EPA statutes is contrary to plain statutory language and legally unsound.

EPA cites only TSCA Sec (6)(b)(4)(D) as a basis for the decision to omit significant exposure pathways. The brief language of that provision, providing for publication of the key elements of a proposed risk assessment, offers no basis to alter the administrator's obligation under Section 6. Indeed, the treatment of risks that may also be subject to other EPA-administered statutes is expressly addressed in TSCA Sec 8(b), which provides:

> "(1) The Administrator shall coordinate actions taken under this chapter with actions taken under other Federal laws administered in whole or in part by the Administrator. If the Administrator determines that a risk to health or the environment associated with a chemical substance or mixture could be eliminated or reduced to a sufficient extent by actions taken under the authorities contained in such other Federal laws, the Administrator shall use such authorities to protect against such risk unless the Administrator determines, in the Administrator's discretion, that it is in the public interest to protect against such risk by actions taken under this chapter. This subsection shall not be construed to relieve the Administrator of any requirement imposed on the Administrator by such other Federal laws.
>
> (2) In making a determination under paragraph (1) that it is in the public interest for the Administrator to take an action under this subchapter with respect to a chemical substance or mixture rather than under another law administered in whole or in part by the Administrator, the Administrator shall consider, based on information reasonably available to the Administrator, all relevant aspects of the risk described in paragraph (1) and a comparison of the estimated costs and efficiencies of the action to be taken under this subchapter and an action to be taken under such other law to protect against such risk."

Further, the specific language of Section 6 provides, in (F) that the administrator is to "integrate and assess available information on hazards and exposures," obviously inclusive of information developed under other EPA statutes.

These provisions clearly establish the role for other EPA programs: information known through other statutory programs shall be considered in the risk evaluation phase for existing chemicals under TSCA, and **after completion of the risk evaluation,** the administrator must follow a process to consider the potential use of other programs **to address the risk under the TSCA standard.** The proposed EPA approach would reverse and fundamentally alter this process.

Further, the omission of important exposure pathways makes it impossible to make the finding required under Sec 6(b)(4)(A) which requires the administrator conduct risk evaluations "to determine whether a chemical substance presents an unreasonable risk…to health or the environment, without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation." "Environment" is defined to include "air, water and land" and the relationship among and between these elements and with "all living things." The statute defines "conditions of use" to mean the circumstances under which the substance is "manufactured, processed, distributed in commerce, used or disposed."

A risk assessment that omits exposures considered under other statutes cannot be assumed to meet this standard. Indeed, other statutory schemes generally do not operate under comparable environmental standards and requirements for consideration. They often require consideration of costs, technical feasibility or other non-risk factors. They are not designed to consider the interaction among air, land and water, but are focused instead on exposure in the specified medium. Consideration of special subpopulations is rarely required and may not even be considered under other statutory schemes. In addition, even when these other regulatory programs are implemented perfectly, they only reduce exposures down to the regulatory standard, they do not eliminate exposures.

TSCA requires specific inclusion of disposal in evaluation of the subject conditions of use; omission of disposal exposures from substances subject to RCRA may have the effect of omitting disposal entirely from the required statutory scope of consideration for the subject conditions of use.

In the case of asbestos, the combination of determining that "legacy uses" are not conditions of use and of omitting disposal because of RCRA regulation has the effect of omitting entirely consideration of disposal, which is specifically enumerated in the statutory definition of conditions of use.

All of these inadequacies make it impossible for the administrator to rely on the work of other regulatory programs to meet the requirements for Section 6 risk evaluations. Indeed, the agency has made no attempt to show any comparability or even consistency between the TSCA risk assessment requirements and the approaches of the regulatory programs associated with these omissions.

Below are two examples from the asbestos problem formulation document that illustrate how legally insufficient the alternative programs can be for this purpose. Congress intended for TSCA to have a risk-based standard and to use this standard to evaluate high priority chemicals that had never been evaluated under other programs based only on risk.

Asbestos air quality regulation dates back to 1986 and is based on an older version of the Clean Air Act (CAA), which did not require consideration of residual risk or all possible exposure pathways. Even if the existing asbestos regulation had been based on the current CAA, it would not be consistent with TSCA's sole focus on health effects. The framework for regulation of hazardous air pollutants under the current CAA is generally fundamentally different from the TSCA process. Hazardous air pollutants (HAPs) are regulated under the CAA in two stages. The first stage is based upon maximum achievable control technology (MACT) within each specific industry. Under MACT, EPA identifies the best performing technologies within an industry and sets a standard based on the performance of these technologies. The cost of achieving such emission reduction and any non-air quality health and environmental impacts and energy requirements, but not risk, are considered at this stage. The second phase of HAP control under

the CAA is a "risk-based" approach in which the risk remaining after the application of MACT is assessed. Within eight years of setting the MACT standards, the CAA requires EPA to assess the remaining risks from each source category to determine whether the MACT standards protect public health with an ample margin of safety and protect against adverse environmental effects. While EPA does not have to consider the costs of any health standards imposed as a result of the risk analysis, it must consider the costs

of a more stringent standard to reduce environmental risks. Furthermore, the residual risk controls only apply to major emission sources; they do not apply to small emitters considered as area sources.

EPA's own discussion of the asbestos requirements under the Resource Conservation and Recovery Act illustrates clearly the gaps between the regulatory approaches to asbestos under RCRA and those required by TSCA. Indeed, the problem formulation document itself makes clear that significant amounts of the considerable quantities of disposal (>25 million pounds) from the on-going asbestos uses are subject only to certain state-level requirements.[14]

The amended TSCA contains new standards for assessment of chemicals, but also a host of new provisions to ensure open processes, fairness and other vital good government goals. The approaches to regulation of asbestos under other statutes generally not only have different substantive standards of review, but also different processes and procedures, especially for the risk assessment aspects of the regulatory process. EPA offers no analysis of the way in which evaluations under other statutes have met the procedural requirements of TSCA.

b. EPA's planned approach to exclude important exposures associated with other EPA-statutes is also scientifically and methodologically unsound.

Risk assessments that are currently available (for appropriate consideration under TSCA Sec 6(F)) are identified in the problem formulation document. Notably, the identified risk assessments under the SDWA and the CAA are from 1985 and 1986 respectively. Nothing under RCRA is identified. Obviously, these programs have not completed risk assessments reflecting changes in the science for more than 30 years. Conclusions based on any such assessments would, at a minimum, require a serious updating of most aspects of the science involved. There is no indication that EPA intends to devote the resources that would be required to update program-specific risk assessments for asbestos even for the narrow purposes of determining whether further action is warranted under such statute. EPA's other regulatory programs have limited resources and many competing priorities, including those required by specific statutory provisions and/or court orders. Congress has provided additional resources specifically for implementation of TSCA, which can compensate for the lack of resources in these other programs. In addition to the advantage TSCA affords EPA to conduct risk assessments and issue regulations covering all sources of exposure, EPA should use the potent information gathering provisions of TSCA 8(a) and 8(d) to update or supplement the risk evaluations conducted under other statutes which are so out of date today. Staff from other program offices should be involved in the assessments conducted under TSCA so they can assist the TSCA program while also updating their media-specific risk evaluations.

c. EPA's planned approach to justify the exclusion of pathways regulated by other programs based on efficiency is flawed.

EPA invokes efficiency as a rationale for its approach to excluding exposures under other statutes. But it is clear that nothing is preventing the agency from making use of prior work conducted under other statutes and the expertise developed throughout the agency. Further, as noted above, TSCA provides a clear path by which the administrator may, after conducting the risk assessment and making the risk findings required by

[14] Asbestos Document, page 44

TSCA, turn to all the other statutes he administers as part of crafting a risk management approach for existing chemicals under TSCA.

This extreme, legally and scientifically unsound refusal to consider significant exposures clearly resulting from current conditions of use is not warranted on efficiency grounds.

3. EPA's Proposed Approach to Risk Evaluation of Pathways Deemed De minimis Is Flawed.

In the carbon tetrachloride problem formulation, EPA asserts without justification that it will exclude multiple uses of the chemical (cleaning and degreasing solvents, adhesives and sealants, paints and coatings) because they pose only de minimis risks. This was the only problem formulation that excluded uses because they were deemed de minimis. While the final chemical risk evaluation rule mentions that de minimis uses could be excluded from consideration, no criteria were provided for determining a use that poses de minimis risks for a chronic toxicant. Since carbon tetrachloride is a carcinogen, EPA must document in the problem formulation the carcinogenic risk level used to designate a pathway as posing de minimis risk. In addition, combined low level exposures resulting from multiple uses and sources of a chemical can result in unreasonable risks to particular subpopulations, so EPA must document that co-occurring de minimis pathways were appropriately evaluated in combination and still found to be below the carcinogenic level of concern if people can experience more than one of these pathways at any given time. Further, the carbon tetrachloride problem formulation should justify why EPA is not using its authority to request new testing by industry to better evaluate these de minimis pathways. The new testing provision of the Chemical Safety Act is clear that the administrator must not interpret the lack of exposure information as a lack of exposure or exposure potential and must seek new information to resolve this issue.

4. EPA's Potential Approach to Rely on OSHA to Regulate Worker Exposure is Flawed.

In addition to the inadequacy of EPA's proposed exclusion of exposures that are "already regulated" by EPA (by statutes other than TSCA, such as the CAA), as discussed above in these comments, this exclusion also reveals a potentially very serious flaw in EPA's methods if the agency intends to apply the same approach to workplace exposures. The Chemical Safety Act requires EPA to consult with OSHA "prior to adopting any prohibition or other restriction relating to a chemical substance with respect to which the Administrator has made a determination to address workplace exposures." So far, the agency has been silent regarding how it intends to address workplace risks, but the strategy of having EPA "punt" its responsibilities regarding workers by transferring them to OSHA is being heavily advocated by industry groups, and it must not remain unchallenged.[15] Any wholesale "referral" to OSHA for potential regulation would in effect leave the workers unprotected, because it is well known that OSHA is unable to promulgate occupational health standards in a timely fashion, if at all.[16]

[15] Submissions to the dicket, TSCA New Chemicals Coalition

[16] GAO report, https://www.gao.gov/products/GAO-12-330 and testimony by Dr. David Michaels, http://democrats-dworkforce.house.gov/imo/media/doc/DMichaels%20Testimony_w.attachments2%2027%202018.pdf

To better understand this concern, it is important to note that all ten chemicals slated for analysis at this stage of the TSCA mandates, and eventually slated for potential regulation, have their highest exposures and pose their most serious risks to workers who manufacture, process, transport, dispose of or otherwise handle these chemicals. This is no surprise: workers are nearly always the first and most seriously exposed populations, experiencing the highest risks. In addition, four of the chemicals are not regulated at all by OSHA, and the remaining six are currently regulated by OSHA standards that are scientifically obsolete, based on studies more than a half century old. Because of OSHA's inability to regulate in a timely manner, referral of the responsibility to regulate these chemicals would condemn workers to significant risks for a long time, or even indefinitely. Table 1 shows the contrast between current OSHA standards for the ten chemicals with more modern standards (Cal-OSHA) or recommendations (NIOSH and ACGIH). It is evident that current OSHA protections are highly inadequate and TSCA regulation will be necessary.

TABLE 1. OSHA PERMISSIBLE EXPOSURE LEVELS COMPARED WITH OTHER STANDARDS/GUIDELINES

CHEMICAL	OSHA Permissible Exposure Level (PEL)	California OSHA Permissible Exposure Level (PEL)	NIOSH Recommended Exposure Level (REL)	ACGIH Threshold Limit Value (TLV)
Asbestos	0.1 fibers/cm^3	0.1 fibers/cm3	0.1 fibers/cm3	0.1 fibers/cm3
1-Bromopropane	None	5 ppm	0.3 ppm	0.1 ppm
Carbon Tetrachloride	10 ppm	2 ppm	Carcinogen*	5 ppm
1,4 Dioxane	100 ppm	0.28 ppm	Carcinogen*	20 ppm
HBCD	None	None	None	None
NMP	None	1 ppm	None	None
Methylene Chloride	25 ppm	25 ppm	Carcinogen*	50 ppm
Perchloroethylene	100 ppm	25 ppm	Carcinogen*	25 ppm
Pigment Violet	None	None	None	None
Trichloroethylene	100 ppm	25 ppm	Carcinogen*	10 ppm

*Lowest Feasible Exposure

While it is commendable that the agency recognizes the workplace hazards posed by these chemicals and intends to evaluate the risks at this stage, it is crucial that EPA state explicitly that it will take steps to make sure that workplace risks are regulated in a timely fashion under TSCA, even as OSHA, NIOSH and other agencies are consulted in the process of doing so, as TSCA allows.

Respectfully submitted,

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APPENDIX 8
Comments on Draft Pigment Violet 29 Risk Evaluation
Under the Toxic Substance Control Act
January 14, 2018

The Environmental Protection Network (EPN) is an organization comprised of over 350 EPA alumni (including scientists, policy specialists and others) volunteering their time to protect the integrity of US Environmental Protection Agency (EPA), human health and the environment. We harness the expertise of former EPA career staff and confirmation-level appointees to provide an informed and rigorous defense against current Administration efforts to undermine public health and environmental protections. We have the following comments on the draft Pigment Violet 29 (PV29) Risk Evaluation Under the Toxic Substance Control Act (TSCA).

On November 14, 2018, EPA published in the Federal Register a draft "TSCA Risk Evaluation for Colour Index (C. I.) Pigment Violet 29 (PV29)." EPA states that the purpose of this risk evaluation is to "determine whether a chemical substance presents an unreasonable risk to health or the environment under the conditions of use, including an unreasonable risk to a relevant potentially exposed or susceptible subpopulation." *EPN believes this purpose is undermined by (1) EPA's use of a flawed systematic review process and discretionary use of said process, (2) refraining from requesting additional public information under the veil of Confidential Business Information (CBI), and (3) overlooking a key pathway for children and pregnant women despite a requirement to protect vulnerable subpopulations.*

1. Use of a Flawed Process

The 2016 TSCA requires the use of the "best available science" and the "weight of the scientific evidence" (section 2625). The latter of which is defined in the regulation as "…a systematic review method, applied in a manner suited to the nature of the evidence or decision, that uses a pre-established protocol to comprehensively, objectively, transparently, and consistently identify and evaluate each stream of evidence, including strengths, limitations, and relevance of each study and to integrate evidence as necessary and appropriate based upon strengths, limitations, and relevance." In not using a systematic review process to evaluate the weight of scientific evidence, EPA limited the science under review and therefor did not use the best available science.

EPN is deeply concerned with two issues: (1) the lack of use of appropriate systematic review methods and (2) the lack of adequate published data. EPA evaluated the relatively sparse datasets that are mainly comprised of CBI data. These datasets consisted of about two dozen studies, all of which were conducted by the chemical's manufacturer or other data owners, most in accordance with Organisation for Economic Co-operation and Development (OECD) test guidelines. EPA should follow the

guidelines in the National Academy of Sciences 2017 report on the Application of Systematic Review Methods.[17]

EPA incorrectly describes its draft 2018 EPA guidance entitled "Application of Systematic Review in TSCA Risk Evaluations" as systematic review, but it does not meet current scientific standards. On August 16, 2018, EPN submitted detailed criticisms of that draft systematic review process. Other scientific groups have similarly criticized the EPA guidance.[18] Our comments (see Appendix 1) documented EPA's failure to follow necessary internal and external peer-review procedures in developing this process, serious flaws permeating the entire TSCA systematic review process, and critical flaws in evaluating individual studies for use in toxicity assessments (such as failure to assess for bias). This draft "Application of Systematic Review in TSCA Risk Evaluation" is inconsistent with best practices in systematic review and should not be used for any purpose.

In this evaluation the agency failed to publish its systematic review protocol in advance. Additionally, minimal effort seems to have been expended on the first three steps of what it considers to be a credible systematic review: (1) *Publish the protocol*, (2) *Data Search*, during which a number of sources are queried to identify potentially useful literature, and (3) *Data Screening*, during which abstracts and full texts of potentially useful literature are examined for relevance (see page 18, paragraph 2 of the draft risk evaluation). EPA incorrectly considers it discretionary when EPA chooses to follow the best scientific practices as required by law or even all of the steps in its own draft guidance entitled "Application of Systematic Review in TSCA Risk Evaluations." EPA laid out a review process in that draft guidance (which our previous comments argue is flawed) but EPA has failed to follow in a vigorous manner said process when evaluating PV29.[19]

EPN would be supportive of using the Office of Research and Development (ORD) systematic review process in evaluating all the studies. EPA's ORD current process is endorsed by National Academy of Science (NAS) and comes closer to the (1) NAS 2014 guidance or the practices used by (2) OHAT, (3) Navigation Guide or other credible approaches to systematic review approaches.[20,21,22,23]

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[17]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: The National Academies Press; 2017. https://doi.org/10.17226/24758

[18]National Academies of Sciences, Engineering, and Medicine. Strategies and Tools for Conducting Systematic Reviews of Mechanistic Data to Support Chemical Assessments. 2018. http://dels.nas.edu/Upcoming-Workshop/Strategies-Tools-Conducting-Systematic/AUTO-5-32-82-N

[19]National Research Council. Review of EPA's Integrated Risk Information System (IRIS) Process. Washington, DC: The National Academies Press; 2014. https://doi.org/10.17226/18764.

[20]National Academies of Sciences, Engineering, and Medicine. Progress Toward Transforming the Integrated Risk Information System (IRIS) Program: A 2018 Evaluation. Washington, DC: The National Academies Press; 2018. https://doi.org/10.17226/25086.

[21]NAS 2014

[22]U.S. Department of Health and Human Services. National Toxicological Program. OHAT Systematic Review. https://ntp.niehs.nih.gov/pubhealth/hat/review/index-2.html

[23]Woodruff, T.J., Sutton, P. An evidence-based medicine methodology to bridge the gap between clinical and environmental health sciences. Health Aff. (Millwood). 30, 931–7. 2011. https://doi.org/10.1377/hlthaff.2010.1219;

2. Insufficient Information

Not having access to the studies used in this review is problematic and should be remedied. EPN is concerned that EPA did not use their TSCA authority, under Sections 4 and 5, to get an appropriate release of key or critical information necessary to allow for critical review of the study methods and conclusions. The 2016 TSCA amendments expanded EPA's chemical testing authority to "obtain testing information for prioritizing or conducting risk evaluations on a chemical." All 24 studies used as the basis for this risk evaluation are company owned, and all data belongs to one or more manufacturing companies. In addition, many of these studies claimed CBI. TSCA section 14(b) identifies several categories of information that may not be protected as CBI, including: "health and safety studies and information from health and safety studies where the chemical or mixture has been offered for commercial distribution or for which testing is required under TSCA section 4 or notification is required under TSCA section 5." These studies must be published for a credible risk assessment and for any credible peer review.

Only the summaries of these CBI studies have been made available to the public, which are insufficient. Without adequate information, the public cannot adequately review this decision. The agency has thus failed to provide notice and comment opportunities. While advisory committees may be cleared for CBI and will have access to the studies for review, this still leaves the public in the dark. In addition, many of these committees are being challenged for conflicts of interest or limiting the usual number of panelists.

A timely example would be the recent shrinking of the Clean Air Science Advisory Committee (CASAC), limiting who may be a member of CASAC based on previous EPA grants, and the disbandment of the Particulate Matter review panel and the decision not to reinstate the Ozone review panel. A group of former CASAC chairs and former CASAC members submitted two comment letters critiquing the lack of expertise on the smaller than usual committee, dissolving additional panels, the shortened and accelerated inadequate timeline, and the new membership criteria which eliminates many qualified individuals.[24,25] They emphasized how procedural issues can have a lasting effect on science, science use, and science-based decisions.

The letter "Withholding of Public Access to Critical Studies on Pigment Violet 29 -- EPA-HQ-OPPT2018-0604" (see Appendix A) lays out similar complaints regarding the availability of industry studies being concealed from the public. On December 6, 2018, the Center for Environmental Health, Earthjustice, Environmental Defense Fund (EDF), the Environmental Health Strategy Center, Natural Resources Defense Council, and Safe Chemicals Healthy Families sent a letter on this same issue to Deputy Assistant Administrator Nancy Beck. An EDF scientist dove in even further in a series of blog posts addressing issues with evaluating exposure, evaluating hazard, and OECD studies being used for

long term projections. The first post examines two 1970s studies done by the company BASF, these studies are the basis for the EPA assertion that ""no adverse effects were observed for" the inhalation route of

[24]Frey, Chris et al. Letter to CASAC from Former Members of 2015-2018 Particulate Matter Review Panel.
[25]Frey, Chris et al. Letter to CASAC from Former Members of 2009-2014 CASAC Ozone Review Panel.

exposure." However, BASF disregarded the adequacy and reliability of their studies due in part to major methodological deficiencies.[26] The second post discusses issues with exposure studies, mainly a questionable value for an "approximate maximum workplace air concentration" to be expected over a 12 hour shift at a PV29 manufacturing facility. This value came from a chemical company and while EPA uses it, they acknowledge they do not know what this workplace air value actually represents (see page 22, paragraph 1 of the draft risk evaluation). The third post expands on the second, explaining further scientific errors. The author claims EPA relied on OECD data which is explicitly not to be used for long term studies investigating chronic effects.[27] EPN agrees that data related to health and safety, addressed directly or indirectly in all 24 PV29 studies, cannot be withheld as CBI under TSCA.

1. Overlooked Pathways

Finally, EPA has not conducted a sufficient review as required by law because it has failed to assess relevant exposure pathways for sensitive populations. Specifically, EPN believes important pathways for the sensitive subpopulation of children have been left out. EPA lists PV29's "industrial and commercial activities/uses" as: processing, paints and coatings, plastic and rubber products, merchant ink for commercial printing and distribution. Paints, art supplies, toys, and food packaging and examples of possible exposure pathways for children. Some of these systematic omissions relate to the flawed "framework" prioritization and evaluation rules that inappropriately limit the exposures EPA considered. In addition, data on PV29 is already limited and sparse, exclusively observing workers likely looks only at adults who are healthy enough to work. Studying adults is not, and has never been, sufficient to understand the impact of chemical exposures for children who may have critical developmental periods when their brains, reproductive organs, and other important systems are developing. Pregnant women (fetus and mother) and children should be separately assessed. Manufacturers should demonstrate adequate data to support a claim of no unreasonable risk. No data does not equate to no risk. EPA must therefore conduct a more serious exposure screening to assess each sensitive subpopulation.

The 2016 TSCA amendments require that EPA specifically consider susceptible subpopulations, as discussed in both the legislation and the introduction of the PV29 draft risk evaluation. TSCA section 6, 15 U.S.C. 2605, requires EPA to conduct risk evaluations to "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible

subpopulation identified as relevant to the risk evaluation by the Administrator under the conditions of use." 15 U.S.C. 2605(b)(4)(A).

[26]Denison, Richard. "Exhibit PV29: Why this EPA can't be trusted to forthrightly assess chemical risks under TSCA." Environmental Defense Fund. 2018. http://blogs.edf.org/health/2018/12/13/exhibit-pv29-why-this-epa-cant-be-trusted-to-forthrightly-assess-chemical-risks-under-tsca/

[27]Denison, Richard. "Correction: The Trump EPA's first TSCA risk evaluation is a skyscraper of cards, not just a house." Environmental Defense Fund. 2018. http://blogs.edf.org/health/2019/01/08/correction-epas-first-tsca-risk-evaluation-is-a-skyscraper-of-cards-not-just-a-house/

As the first draft risk evaluation to be published, it is important to recognize and understand the flawed procedure used in this instance. The procedure should not be repeated moving forward with the other nine risk evaluations - or any others in the future. EPA should have a consistent procedure for conducting systematic reviews and conducting risk evaluations.[28,29]

Respectfully submitted,

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These comments were prepared by Barbara Elkus, Penny Fenner-Crisp, Trish Koman, and Betsy Southerland on behalf of the Environmental Protection Network. Questions should be addressed to Betsy Southerland, easydee420@gmail.com.

[28]NAS 2017.
[29]National Research Council. Science and Decisions: Advancing Risk Assessment. Washington, DC: The National Academies Press; 2009. https://doi.org/10.17226/12209.

Appendix A
Letter to Deputy Assistant Administrator Dr. Nancy Beck Re: Withholding of Public Access to Critical Studies on Pigment Violet 29

December 6, 2018 Dr. Nancy Beck Deputy Assistant
Administrator Office of Chemical Safety and Pollution
Prevention U.S. Environmental Protection Agency 1200
Pennsylvania Avenue, NW Washington, D.C. 20460
Re: Withholding of Public Access to Critical Studies on Pigment Violet 29 -- EPA-HQ-OPPT-2018-0604

Dear Dr. Beck:

Our organizations are deeply concerned that EPA is withholding from the public 24 studies that form the basis for its draft risk evaluation on Pigment Violet 29 (PV29). Failure to release these studies violates section 14 of the Toxic Substances Control Act (TSCA), reflects a troubling lack of transparency, and will frustrate the ability of interested parties to review and submit comments on the science EPA cites to support its risk evaluation and to participate meaningfully in the peer review process. We request that the 24 studies be placed in the docket for the draft risk evaluation without delay.

The 24 studies, conducted by PV 29's manufacturers, address its physical and chemical properties, environmental fate, human health effects and toxicity to aquatic organisms. According to the draft risk evaluation, 20 of the studies were submitted to the European Chemicals Agency (ECHA) in support of registration under the European Union (EU) REACH Regulation. The other four studies were not provided to ECHA but were apparently submitted to EPA by an unnamed data owner. EPA has made available the "robust summaries" prepared by the data owners for the 20 studies submitted to ECHA, but has withheld all 24 studies based on "a claim of business confidentiality by the data owners."

Under section 14(b)(2), the law's restrictions on disclosure of confidential business information (CBI) do not apply to "any health and safety study which is submitted under this Act" for a chemical substance which "has been offered for commercial distribution." The absence of CBI protection extends to both the study itself and "any data reported to, or otherwise obtained by, the Administrator from" the study.

Section 3(8) of 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 underlying information and...toxicological, clinical and ecological studies..." EPA regulations at 40 CFR 716.3 state that "[i]t is intended that the term health and safety study be interpreted broadly" and encompass "[a]ny data that bear on the effects of a chemical substance on health or the environment." The regulations are explicit that tests to determine the chemical and physical properties and fate and transport behavior of a substance fall within the definition, along with studies of a chemical's human health effects and
eco-toxicity.

Thus, the 24 studies on PV29 are "health and safety studies" that cannot receive CBI protection under TSCA. Moreover, EPA's obligation to disclose these studies cannot be satisfied merely by releasing "robust summaries" but requires public access to the full studies.

EPA has not described the claim(s) of confidentiality which it believes justifies withholding the 24 studies, but with respect to chemical substances, the only portion of a health and safety study that can be treated as CBI under section 14(b)(2) is information "that discloses processes used in the manufacture or processing of a chemical substance." The 24 studies likely contain little, if any, information meeting this description, and in the unlikely event any of the studies contain legitimate and substantiated CBI of this type, it can be redacted while all health and safety information is disclosed as provided for in section 14(b)(1).

It is possible that the data owners are basing their CBI claims on their "proprietary interest" in the studies under REACH. However, EPA could only honor these CBI claims if they have a basis in section 14 of TSCA. Nothing in section 14 allows EPA to avoid its unconditional obligation to disclose health and safety studies because of property right claims under European Union (EU) law.

EPA has suggested that public access to the 24 studies is unnecessary because it "has confirmed that the results of these full study reports are consistent with the corresponding robust summaries available in ECHA." However, this puts the public in the untenable position of accepting EPA's findings on faith. Without access to the full studies, the public cannot form its own judgments about the quality of the studies and the proper interpretation of the results. Thus, the public cannot meaningfully comment on whether EPA's reliance on the studies is justified and whether they in fact support the Agency's conclusion that PV29 does not present a risk of harmful effects on health and the environment. EPA's withholding of the studies effectively shuts the public out of the comment process because the 24 studies comprise the *sole* scientific basis for EPA's determination that PV29 is not toxic to humans or aquatic species.

EPA's indication that it will allow members of the Scientific Advisory Committee on Chemicals (SACC) to review the 24 studies but deny access to the public only compounds this lack of transparency. An essential element of peer review under EPA's Peer Review Handbook is a process to provide public input to the reviewers. This will be impossible if the public lacks access to the 24 studies. Moreover, by treating portions of the peer review process as CBI, EPA will deny the public full access to the peer reviewers' conclusions and recommendations on a central element of the PV29 evaluation, further blocking meaningful public participation in the review process. It also will constrain the peer reviewers' ability to engage in a robust debate and discussion during the peer review process.

It is ironic that EPA believes it can base regulatory decisions on PV29 on data that are unavailable to the public while taking a diametrically opposite position in its recent proposed rule purportedly promoting "transparency" in regulatory science. 83 Federal Register 18768 (April 30, 2018). EPA based that proposal on the principle that "[b]y better informing the public, the Agency in [*sic*] enhancing the public's ability to understand and meaningfully participate in the regulatory process" and that "EPA

should ensure that the data and models underlying scientific studies that are pivotal to the regulatory action are available to the public... in a manner sufficient for independent validation." While our groups have criticized many aspects of the April 30 proposal, EPA's contradictory and selective adherence to its own transparency goals is deeply troubling.

For these reasons, we urge you to place the 24 studies in the docket for the PV29 risk evaluation without delay. We are simultaneously filing a request for the studies under the Freedom of Information Act (FOIA) to preserve our ability to access them in the event EPA does not respond favorably to this letter. Please contact SCHF counsel Bob Sussman with any questions at bobsussman1@comcast.net.

Respectfully submitted,

Ansje Miller, Director of Policy and Partnerships **Center for Environmental Health**

Jonathan Kalmuss-Katz, Staff Attorney **Earthjustice**

Richard Denison, Lead Senior Scientist **Environmental Defense Fund**

Patrick MacRoy, Deputy Director **Environmental Health Strategy Center**

Daniel Rosenberg, Senior Attorney **Natural Resources Defense Council**

Elizabeth Hitchcock, Director **Safer Chemicals Healthy Families**

cc: Charlotte Bertrand, Acting Principal Deputy Assistant Administrator
Erik Baptist, Deputy Assistant Administrator Jeff Morris, Director OPPT Tala Henry, Deputy Director OPPT Lynn Vendinello Cathy Fehrenbacher David Fotouhi, Esq. Dr. Todd Peterson Dr. Stan Barone

APPENDIX 9
TESTIMONY FOR THE PUBLIC MEETING OF THE SCIENCE ADVISORY COMMITTEE ON CHEMICALS (SACC)
COMMENTS BY GARY E. TIMM ON BEHALF OF THE ENVIRONMENTAL PROTECTION NETWORK

June 20, 2019

Good morning. It is a pleasure to be here. I think that my perspective is unique and hope that it is helpful to the Committee. My name is Gary Timm. I worked at EPA for 38 years and retired in 2011. I was chief of the Chemical Testing Branch in the Office of Pollution Prevention and Toxics for 10 of those years. The Chemical Testing Branch is responsible for implementing the testing provisions of Section 4 of the Toxic Substances Control Act (TSCA). I am also a member of the Environmental Protection Network (EPN), a non-profit organization comprised of over 450 former EPA employees volunteering their time to protect the integrity of EPA and provide an informed and rigorous defense against the current Administration's efforts to undermine the protection of public health and the environment.

Today, I want to share my experience with the old TSCA to underscore how EPA today is failing to use the authority Congress has recently given it in the new TSCA to require robust test data to inform its risk evaluation of existing chemicals, including PV29.

In 2016 the Congress amended TSCA to give EPA more authority and correct many of the features of the Act that gave us so much difficulty in doing our job. When I started out as branch chief, the only avenue we had to require industry to test the chemicals they manufactured or processed was to make three legal findings, analyze the cost impact of requiring testing, issue a proposed rule, take public comment, and then issue a final rule to require testing. The three findings, which are still in the Act, are

1. Either find that the chemical may present an unreasonable risk to human health or the environment, or that it is produced in substantial quantities and would result in significant or substantial human exposure or substantial environmental release,

2. That data were insufficient to reasonably assess or predict the effects of the chemical, and

3. That testing was necessary to generate the needed data.

These findings were difficult, and time and resource consuming to make. We could not find that a chemical "may present an unreasonable risk" without locating an existing significant toxicity study and demonstrating the potential for human exposure or environmental release. Alternatively, for high production volume chemicals, we could demonstrate substantial or significant human exposure or substantial environmental release to make the first finding.

Making the second finding meant that we had to conduct a wide search for all available studies as well as collect unpublished data using our authority under section 8(d) and critically review each study to determine its inadequacy before we could require testing for a particular endpoint. Under optimum

conditions, we could issue the final rule to require testing two years after we started the process. Typically, it was years longer. A proposal developed by the Natural Resources Defense Council and the Chemical Manufacturers Association to substitute Negotiated Consent Agreements for this long process helped somewhat, but disagreements between the agency and industry sometimes generated no time savings at all. The situation was so dire that when data were needed by another office in EPA or another agency, we effectively ceded routine testing of industrial chemicals to the National Toxicology Program (NTP) because we could not meet our potential client's timelines. This testing by the NTP was paid for by the taxpayer instead of being paid by industry under TSCA, which was the intent of Congress in passing the law.

This is no longer the situation. The Lautenberg Amendments gave EPA authority to require testing by rule, order, or consent agreement if data were needed to conduct a risk evaluation or even to establish the priority of a chemical for risk evaluation. Many commenters have noted the paucity of studies in the PV29 database. There is, in my mind, a disconnect between EPA's selection of PV29 for the TSCA work plan and the conclusions of the draft risk evaluation that PV29 is relatively inert and presents no unreasonable risks. Several commenters, including EPN, have expressed concern that EPA relied on inadequate data to reach this conclusion, and that the studies that they did rely on were not fully disclosed to the public as required by TSCA.

For PV29, EPA has based its conclusion of "no unreasonable risk" on claims of low exposure, low bioavailability, and low toxicity observed only in short-term studies. These data seem to support a hypothesis of low risk, but are woefully insufficient to establish it. As tiered testing is encouraged by TSCA, EPA should confirm this hypothesis by requiring workplace monitoring, basic pharmacokinetic (PK) data measuring levels of PV29 in blood and distribution in fat, and a 90-day subchronic test as directed by the PK results. Further testing may be necessary based on the outcome of these tests. In addition, EPA noted that PV29 was expected to partition to soil and sediment. It therefore has no basis to conclude that there is no unreasonable risk to the environment without biodegradation data and data on the toxicity to benthic organisms.

The risk evaluation of PV29 is critical because it will be seen as precedent setting. EPA needs to establish criteria to determine the minimum data set necessary to make a risk determination. Without such criteria, it looks like an arbitrary judgment call on each chemical. With the new authority EPA has under TSCA, EPA has an obligation to require testing for PV29 to meet the minimum data requirements and fill critical data gaps before making a risk evaluation.

EPA's primary obligation is to ensure that any finding of "no unreasonable risk" is based on data that actually show no risk, as opposed to being based on the absence of data. Mandating testing is one way to fill data gaps, and we urge EPA to do this, but the most critical point for the SACC is that EPA cannot make risk determinations without actual data showing no unreasonable risk.

As EPN's formal comments submitted on May 17, 2019, expressed, we are concerned about the following:

1) The lack of transparency in this risk evaluation will create a precedent of making "no unreasonable risk" determinations based on proprietary information.

2) The most critical study in this evaluation was heavily redacted, which removes the ability to do an independent analysis.

3) A potentially useful and important study was not included in the draft risk evaluation, with no explanation.

Thank you for the opportunity to speak today.

APPENDIX 10

Review of (Some of) the Recently Released BASF Pigment Violet 29 Studies

May 17, 2019

The Environmental Protection Network (EPN) is an organization comprised of over 400 EPA alumni volunteering their time to protect the integrity of U.S. Environmental Protection Agency (EPA), human health and the environment. We harness the expertise of former EPA career staff and confirmation-level appointees to provide an informed and rigorous defense against current Administration efforts to undermine public health and environmental protections.

We have the following concerns:

1) The lack of transparency in this risk evaluation will create a precedent of making "no unreasonable risk" determinations based on proprietary information.
2) The most critical study in this evaluation was heavily redacted, which removes the ability to do an independent analysis.
3) A potentially useful and important study was not included in the draft risk evaluation, with no explanation.

Introduction

On November 15, 2018, EPA's Office of Pollution Prevention and Toxics (OPPT) issued a draft risk evaluation for Pigment Violet 29 (PV29) for public review and comment (see Appendix 8). It was the first of the initial 10 chemicals to undergo a draft risk evaluation by this Administration under the new priority-setting/evaluation system for existing chemicals implemented in response to mandates in the 2016 updated Toxic Substances Control Act (the "new" TSCA). Unlike the other nine substances on the initial top 10 list—Asbestos; 1-Bromopropane; Carbon Tetrachloride; 1, 4 Dioxane; Cyclic Aliphatic Bromide Cluster (HBCD); Methylene Chloride; N-Methylpyrrolidone; Perchloroethylene; and Trichloroethylene—PV29 has received little prior agency or public attention. Furthermore, unlike the other nine on the list, it is a substance for which the extant database is constituted solely of toxicity, physical/chemical characteristics, and environmental fate studies declared by its manufacturer (BASF) to be Confidential Business Information (CBI). As a result, a somewhat non-traditional approach needed to be taken by EPA in order to develop a hazard and risk assessment.

PV29 is one among many substances that are registered in the European Union's Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) program. REACH establishes procedures for collecting and assessing information on the properties and hazards of substances. Data requirements are standardized, driven by the amount of product manufactured and/or imported on an annual basis. As one might expect, as the production/import volume increases, so does the number and nature of the data requirements. Companies can satisfy these requirements by submitting studies from the open peer-reviewed

literature, from other confidential or open sources using a read-across approach and/or conducting new studies to fill remaining data gaps. The European Chemicals Agency (ECHA) is responsible for the review of submissions and maintenance of the REACH database. In the case of PV29, ECHA reviewed roughly 20 submitted CBI studies, prepared "robust summaries" of each and uploaded their findings into a publicly available database.

EPA's OPPT also has access to the summary and study reports that went to ECHA for REACH registration plus several others that had been conducted for other purposes. EPA screened all but one of the REACH studies for the quality of the methods and reporting of results of the individual studies, citing each in the draft evaluation. EPA concluded that the 24 studies it reviewed were of high or medium quality and would be suitable for use in the risk evaluation. Rather than preparing their own summaries of each study, they determined that the ECHA robust summaries adequately captured the findings of the CBI studies and referenced them instead. They did so in a manner similar to that which they and other agency program offices have historically used the Office of Research and Development's (ORD) Integrated Risk Information System (IRIS) hazard assessments as the basis for the hazard component of their programs' risk assessments. As such, this was not as significant of a departure from a common practice than some might assert. ECHA staff scientists possess a level of expertise at a minimum equivalent to EPA staff, so this seemed to be a reasonable and efficient approach to take.

Setting an Unwanted Precedent

EPN has compiled these comments primarily because we are concerned about precedent setting. TSCA gives EPA the authority to require testing that will not be held as CBI before they make a determination of "no unreasonable risk." EPA is not using that authority in this case, and presumably won't do so in future cases. Generally, whether the agency is determining there is risk or no risk, it's important to be able to see the data. That said, it's particularly important for the protection of public health and the environment when a "no unreasonable risk" determination is made.

In the case of PV29, making these data fully available may or may not change EPA's determination, but for other chemicals in the pipeline, relying heavily on confidential data might make a significant difference. EPN urges the agency to use its authority and not make a determination based on proprietary information.

Critical Study Was Heavily Redacted

There have been calls from several sources for the release of all original full study reports for PV29. BASF (and EPA) acquiesced, somewhat. EPA released documentation on the studies in March 2019, but portions of all of the full study reports were redacted. In all cases, redaction obscured the names of individuals involved in the conduct or quality assurance (QA) of the study or were a supply source or testing lab. EPN does not believe this has an impact on the ability to review and assess the study for quality and results. However, in one case, the degree of redaction was far more significant (Study #17, the rat reproduction/developmental screening study). What remains in this case are the summary data for each parameter measured, as is true for all the other studies, but the raw data for each individual animal, which form the basis of the summaries, is blacked out. So, in this case, although one can judge the quality and

integrity of the results of the study, reach conclusions, and do the side-by-side comparison with the related test guideline, one cannot conduct an independent analysis of the data. In addition, no justification was provided for redacting the individual animal data; health and safety studies such as this one, information from health and safety studies, and certain other information, may not be protected as CBI under TSCA.

Potentially Useful Study Was Not Included

Without explanation,EPA did not include a review of, or reference to, a 90-day repeated dose dietary study in rats that also is in the REACH database for this chemical. While this study likely would not have been deemed pivotal for use in characterizing a no-observed-adverse-effect-level (NOAEL) or calculating a margin of exposure, it would have contributed to the weight-of-evidence conclusion that this chemical possesses low hazard and risk potential.

Summary of Findings

We were curious to find out if having access to the full study reports would make any difference in the conclusions reached after reviewing only the robust summaries. That said, EPN members confined their review to those toxicity studies most relevant to human hazard assessment, given that this is where we had the most expertise available.

Studies reviewed:

Studies with summaries only:

- Study #1 Eye Irritation (1975)
- Study #2 Eye Irritation (1978)
- Study #5 Inhalation toxicity study in rats (1975)
- Study #6 Inhalation toxicity study in rats (1978)
- Study #7 Acute intraperitoneal toxicity in mice (1975)
- Study #8 Acute intraperitoneal toxicity in mice (1978)
- Study #9 Acute oral toxicity in rats (1975)
- Study #10 Acute oral toxicity in rats (1978)
- Study #12 Skin irritation study in rabbits (1975)
- Study #13 Skin irritation study in rabbits (1984)

Studies with full reports (but partial redaction):

- Study #3 Acute dermal irritant effects/caustic effects on the rabbit eye (Rupprich and Weigand, 1984)
- Study #4 Acute irritant effects/caustic effects on the rabbit eye (Rupprich and Weigand, 1984)
- Study #11 Acute Oral Toxicity (Acute oral toxicity in the male and female Wistar rat (Rupprich and Weigand, 1984)
- Study #14 Study of mutagenic potential in strains of Salmonella typhimurium (Ames test) and E. coli (1983)
- Study #15 Gene Mutation Assay in Chinese Hamster V79 cells *in vitro* (2012)

Study #16 Skin sensitization: Local Lymph Node Assay (mouse) (1999)

Study #17 Reproduction/developmental Toxicity Screening Test in Wistar Rats Oral Administration (Gavage) (2013)

Study NOT included in EPA evaluation:

Study X: 90-day repeated dose, subchronic study in rats (ECHA robust summary only)

Studies not reviewed:

Study #18 Acute Toxicity Zebra Danio (1988)
Study #19 Lemna Gibba Growth Inhibition Test (2012)
Study #20 Daphnia Magna Acute Immobilization Test (2012)
Study #21 Determination of Inhibition of Oxygen Consumption by Activated Sludge (1999)
Study #22 Determination of Biodegradability (1999)
Study #23 Physical Chemical Properties-Log_{KOW} (2013)
Study #24 Physical Chemical Properties-Melting Point (2013)

Approach to review

The review was conducted in three phases.

- Phase 1: Review each study and capture key elements and results. Note agreement or disagreement with study authors' conclusions.
- Phase 2: If an Organization for Economic Cooperation and Development Test Guidelines (OECD TG) was followed, compare elements of the conduct and reporting of the study with requirements/preferences in the TG to judge conformance with the TG.
- Phase 3: Review related ECHA robust summary, if available, to determine similarities or differences between our review and theirs.

Findings

Our assessments of each of the 17 studies reviewed (and included in the EPA evaluation) was consistent with that of ECHA's, with the minor exception of the resulting calculated LD50 in Study #8 (Acute intraperitoneal toxicity in mice). We concluded the LD50 $\geq$ 10,000 mg/kg. ECHA accepted the study report's finding of ~9000 mg/kgbw—a difference of no importance in classification of the endpoint or the overall importance of this study in the assessment of human health because no one is likely to be exposed to this substance by this route in the real world.

A brief word about Study X—the 90-day repeated dose study in rats. This was an old study (1967); therefore, it was not run under Good Laboratory Practice (GLP) or a formal test guideline. Nonetheless, it did possess sufficient integrity so that ECHA declared it a key study at Level 2 (reliable with restrictions), a designation shared by a number of the other 20 ECHA REACH studies that EPA used. Of importance are the reported results: no systemic toxicity effects were seen in male or female rats after 90days of dosing via

the diet at either 500 or 1000 mg/kg/bw/day, a finding consistent with the results of Study #17 (the reproductive/developmental toxicity screening test), that is, the NOAEL $\geq$ 1000 mg/kgbw/day.
Based upon our review, we are not particularly concerned about having only summaries of the 10 short-term assays. We could assess the available information adequately, as little more useful information would have been found in a full study report. The raw data for each animal in each study were included in data tables for all of the studies. Most of these studies are over 30 years old, with seven being conducted before consensus test guidelines were available and/or GLP guidelines were implemented. Documentation was more unstructured and sparse in those days. There are three exceptions. Studies #3, #4 and #13 were conducted after an OECD test guideline became available (OECD TG 404 and 405, each first issued in 1981). Studies #3 and #4 reference the OECD TG they followed (TG 404 and 405, respectively). While the summary of Study #13 makes no reference to any test guideline, the information available suggests that it was conducted in a manner consistent with OECD TG 404, including preferred test species, number of test animals, exposure, and observation durations and documentation of test results in tabular form. Given the amount of information available from each of these 10 studies, there is no reason to exclude them from contributing to the characterization of the substance's hazard profile.

In reviewing the other studies, we found the full reports, too, provided more than enough information to judge the integrity of the study and provide the ability to reach conclusions about the results and their importance. The side-by-side comparison of the study report with the relevant TG shows study compliance with that guideline in all cases.

APPENDIX 11

Andrew Wheeler, Administrator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20004

October 18, 2019

Re: Imminent and Serious Health Risks from Acute Consumer and Worker Exposure to 1-Bromopropane

Dear Administrator Wheeler:

The Environmental Protection Network (EPN) is an organization comprised of over 450 U.S. Environmental Protection Agency (EPA) alumni volunteering their time to protect the integrity of the EPA, human health and the environment. We harness the expertise of former EPA career staff and confirmation-level appointees to provide an informed and rigorous defense against current Administration efforts to undermine public health and environmental protections.

We are writing to you to express our concern about the serious health risks demonstrated in EPA's draft risk evaluation for 1-Bromopropane (1-BP) under the Toxic Substances Control Act (TSCA). The draft evaluation concludes that 1-BP presents an unreasonable risk to workers and consumers for developmental and reproductive toxicity from acute exposure. This conclusion is alarming for the following reasons:

1. Our understanding of the risks from developmental effects is that a single exposure during a critical window of vulnerability can adversely impact the fetus and these effects can be irreversible and permanent.
2. The draft risk evaluation shows that workers and consumers are exposed to 1-BP at levels close to and in some cases higher than the levels at which 1-BP has demonstrated adverse developmental effects in toxicology studies.
3. According to the risk evaluation, women of childbearing age comprise half of the large population of consumers, by-standers and workers that are exposed to 1-BP. It is likely that neither consumers nor workers are aware of these risks, and acute exposures greatly exceeding safe levels are associated with the use of 1-BP in spray adhesives, degreasing, and dry-cleaning operations.
4. The usual timeline for completion of the risk evaluation and regulatory action under TSCA is several years, which will continue to leave vulnerable populations exposed to 1-BP and at risk of these serious effects for an inordinate period of time.

5. In addition to the reproductive and developmental effects noted above, exposure to 1-BP can also result in cancer, neurological effects, and liver and kidney toxicity.

Under TSCA section 6(a) (15 U.S.C. 2605(a)), if EPA determines after a risk evaluation that a chemical substance "presents an unreasonable risk of injury to health or the environment, without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation, under the conditions of use," EPA must by rule "apply one or more requirements to the extent necessary so that the chemical substance or mixture no longer presents such risk." TSCA Section 6(d) gives EPA authority to declare a proposed rule under section 6(a) immediately effective when it is "likely to result in an unreasonable risk of serious or widespread injury to health" before completion of the rulemaking process.

While we recognize that EPA's risk evaluation is only a draft, it is extremely unlikely that EPA will change its conclusions regarding the acute risks posed by 1-BP in its final risk evaluation. Therefore, we urge EPA to regulate the hazards of 1-BP in two separate stages. The first stage should begin now, even while EPA is finalizing the risk evaluation, and should focus on the acute reproductive and developmental hazards posed by 1-BP. The first stage should:

- Use an immediately effective final rule under section 6(d) to ban 1-BP from consumer products and to prohibit commercial use of 1-BP in vapor degreasing and dry-cleaning solvent applications.
- Require downstream notification of this prohibition throughout the supply chain.
- Require warnings of the risks to women of reproductive age from 1-BP exposure on labels and safety data sheets for the remaining 1-BP products in commerce.
- Place 1-BP on the "risk list" authorized by section 5(b)(4) as a chemical that "present[s] or may present an unreasonable risk to human health and the environment."

The second stage of regulation should be focussed on remaining uses of 1-BP that are not restricted in the first stage. These uses should be regulated to the extent necessary to eliminate unreasonable risks, including cancer and neurotoxicity effects from chronic exposure. These restrictions should be imposed through the normal TSCA section 6(a) rulemaking process.

It is worth noting the similarity of 1-BP to trichloroethylene (TCE), a chemical already assessed for unreasonable risk under TSCA for which EPA has initiated regulatory action under section 6(a) . Like 1-BP, TCE's is used as a degreasing agent, drycleaning solvent, and in consumer aerosols. Like 1-BP, the driving effect for TCE is developmental toxicity. Other effects of TCE include cancer, neurotoxicity, and kidney, reproductive, endocrine and liver toxicity -- end-points that are also of concern for 1-BP.

In early 2017, EPA proposed two section 6(a) rules for TCE. The first would determine that the use of TCE in vapor degreasing presents an unreasonable risk of injury to health. Accordingly, it seeks to prohibit the manufacture (including import), processing, and distribution in commerce of TCE for use in vapor

degreasing; to prohibit commercial use of TCE in vapor degreasing; and to require manufacturers, processors, and distributors (except for retailers) to provide downstream notification of this prohibition

throughout the supply chain (*e.g.,* via a Safety Data Sheet (SDS)), and to keep records. EPA stated that this supply chain approach is necessary so that TCE no longer presents the identified unreasonable risks. EPA's second TCE proposal would determine that use of TCE for aerosol degreasing and spot removal in dry cleaning operations also presents an unreasonable risk to health and should likewise be banned. Similar to the first rule, the proposed rule would impose these prohibitions at all levels in the supply chain.

Because TCE and 1-BP compete in degreasing, dry cleaning and consumer aerosol applications and have very similar risk profiles, EPA should align its actions on these two solvents so that restrictions on 1-BP do not simply have the effect of increasing use of TCE. EPA's delay in finalizing its two TCE proposals is concerning and unjustified in light of TCE's serious risks. EPA should issue final TCE rules at the same time that it implements the first stage of 1-BP restrictions described above.

Respectfully submitted,

Michelle Roos
Executive Director
Environmental Protection Network

cc: Alexandra Dunn
David Fischer
Jeff Morris
Mark Hartman
Tala Henry
Cathy Fehrenbacher
Stan Barone