

March 20, 2017

**Comments from Academics, Scientists and Clinicians  
on EPA's Procedures for Chemical Risk Evaluation  
Under the Amended Toxic Substances Control Act**

EPA-HQ-OPPT-2016-0654  
FRL-9957-75

Comments submitted to EPA-HQ-OPPT-2016-0636 and by email to Susanna W. Blair, Immediate Office, Office of Pollution Prevention and Toxics, Environmental Protection Agency, 1200 Pennsylvania Ave. NW., Washington, DC 20460-0001; telephone number: (202) 564-4371; email address: [blair.susanna@epa.gov](mailto:blair.susanna@epa.gov).

These comments are submitted on behalf of the undersigned academic, scientists, and clinicians from universities and non-governmental organizations (NGOs) across the U.S. and worldwide. We collectively declare that we have no direct or indirect financial or fiduciary interest in the manufacture or sale of any chemical under consideration of these risk evaluations. The co-signers' institutional affiliations are included for identification purposes only and do not necessarily imply any institutional endorsement or support, unless indicated otherwise.

We have come together to recommend that the U.S. Environmental Protection Agency (EPA) implement the new Lautenberg amendments to the Toxic Substances Control Act (TSCA) in a manner that will ensure the strongest possible protection of human health consistent with EPA's overall mission of protecting human health and the environment and its specific obligations under this statute.

EPA's choices about how to implement the new Lautenberg amendments to TSCA will irrevocably impact the nature and extent of industrial chemicals in our air, water, food, and consumer products, and thus will have a lasting impact on the health of every single American. EPA's actions under TSCA will inevitably determine America's children's exposure to industrial chemicals for generations to come. They will also impact occupational exposures to industrial chemicals in manufacturing, processing, distribution and recycling facilities across the nation and have implications for fenceline communities living near these facilities. Furthermore, EPA's decisions for implementing TSCA will impact the knowledge base about chemical hazards and risks that consumers, state and local government, businesses, and the marketplace rely on for decision-making.

In short - EPA's first precedential decisions on TSCA implementation will set the stage for U.S. chemical policy for decades to come. The consequent health impacts of EPA's decisions – for better or worse – will be borne by American children, workers, families, and communities.

With so much at stake, we welcome EPA's engagement with the public in this process and we offer EPA concrete approaches to embed the most current scientific principles in its methods to assess the hazards and risks of environmental chemicals.

The new Lautenberg amendments to TSCA present an important opportunity for EPA to update their scientific approaches to evaluating risks posed by industrial chemicals in commerce, and to overcome the inadequacies of the original 1976 TSCA law which was universally recognized as weak and ineffective—and which has produced a state of affairs characterized by Carl Cranor, a professor at the University of California, Riverside, as allowing all Americans to be “legally poisoned.”

Our recommendations on EPA's Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act are as follows:

- 1. Implement the strongest human health protections as required by the statute and consistent with EPA’s mission.**
- 2. Protect the health of susceptible populations by including the language proposed by EPA to ensure that all susceptible populations are considered.**
- 3. Fully account for aggregate and cumulative exposure to chemicals and also non-chemical stressors.**
- 4. Improve the clarity and scientific basis of EPA’s description of “factors (considered) in determining unreasonable risk.” While we support that EPA’s decision to not codify a definition for “unreasonable risk,” we strongly support characterizing cancer and non-cancer “hazard” and not “risk” in these factors.**
- 5. Use health-protective default values to reflect and account for the range of variability and susceptibility anticipated in the population.**
- 6. Incorporate the knowledge and perspective of vulnerable populations into EPA’s risk assessment.**
- 7. Remove all language and reference to Margin of Exposure as it represents an outdated scientific approaches to assessing risks for noncancer health effects.**
- 8. Do not codify the weight of evidence (WOE) process but do clarify the definition of the term WOE in the background section.**
- 9. Do not conflate hazard assessment with risk assessment.**
- 10. Increase transparency.**
- 11. Do not equate Good Laboratory Practice (GLP) with study quality.**
- 12. Correct an error in stakeholder feedback section.**

Further details on each of these recommendations are provided below.

Finally, we appreciate that EPA has included following language acknowledging ours and other previous public comments and recommend that it be included in the final rule:

“A number of commenters emphasized the need for EPA to maximize transparency throughout the evaluation process. The EPA received a number of comments about the science used to inform individual risk evaluations, including the types of data, models, policy assumptions (*e.g.*, default factors) and computational approaches. A number of commenters argued that a lack of data does not equate to a lack of risk.”

We are appreciative of the opportunity to provide public input and we look forward to continuing to participate in such opportunities in the near future. Please do not hesitate to contact us with any questions regarding these comments.

Sincerely,

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## **Detailed Comments from Academics, Scientists and Clinicians on EPA’s Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act**

### **1. Implement the strongest human health protections as required by the statute and consistent with EPA’s mission.**

As required under section 6(b)(4) of the Toxic Substances Control Act (TSCA),<sup>1</sup> we support EPA’s proposal to establish a process for conducting 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, under the conditions of reasonably foreseen uses. In establishing this process, EPA must consider the strongest possible protections of human health as allowed under the law. Our comments detailed below are specific ways that EPA can achieve the statutory intent of human health protection.

### **2. Protect the health of susceptible populations by including the language proposed by EPA to ensure that all susceptible populations are considered.**

The law requires EPA to consider potentially exposed susceptible subpopulations in its implementation of TSCA. We strongly support the language proposed by EPA in the Federal Register in relation to “potentially exposed or susceptible subpopulation[s]” specifically the inclusion of the phrase “including but not limited to” before the specific subpopulations identified in the statutory definition. We also strongly support EPA’s proposal to “include specific authorization for EPA to consider both intrinsic (*e.g.*, life stage, reproductive status, age, gender, genetic traits) and acquired (*e.g.*, pre-existing disease, geography, socioeconomic, cultural, workplace) factors when identifying this population.” EPA’s choice is supported by strong scientific evidence that intrinsic and extrinsic factors can make an individual more susceptible to exposure to and harm from toxic chemicals (for example, see the National Academy of Sciences’ (NAS) report *Science and Decisions*)<sup>2</sup>. Risk assessments under a unified approach needs to quantitatively incorporate these intrinsic and extrinsic factors to prevent a systematic underestimation of risk.

### **3. Fully account for aggregate and cumulative exposure to chemicals and also non-chemical stressors.**

*Aggregate exposures:* EPA’s risk evaluation needs to fully account for the fact that people are often simultaneously exposed to the same chemical substance from multiple products and sources across many exposure routes and multiple pathways in the real world. We support EPA’s definition of aggregate exposures and strongly support the incorporation of these aggregate exposures when evaluating risk for the population. Under the law, EPA is required to collect information on uses, taking into consideration relative durations, intensity, frequency, and number of exposures under conditions of use (which includes reasonably foreseen uses), so we encourage EPA to utilize these data and information to account for aggregate exposures in its risk evaluations.

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<sup>1</sup> 15 U.S.C. § 2605(b)

<sup>2</sup> National Research Council. Committee on Improving Risk Analysis Approaches Used by the U.S. EPA, Board on Environmental Studies and Toxicology, Division on Earth and Life Studies. 2009. *Science and Decisions: Advancing Risk Assessment*. Washington, D.C.: National Academies Press.

*Cumulative exposures:* EPA’s risk evaluation also needs to fully account for the reality that people can be exposed to multiple chemicals as well as non-chemical stressors that can add to the same adverse health effect, and needs to be taken into account in the risk assessment process as recommended by the NAS in their Phthalates and Cumulative Risk report.<sup>3</sup> As described below, EPA can use “default values” to account for cumulative exposures.

Additionally, EPA proposes definitions for ‘aggregate exposure’, ‘sentinel’, ‘pathways’ of exposure, ‘routes’ of exposure, ‘variability’ and ‘uncertainty’. We support the proposed definitions for all of the above except for “sentinel exposure” and “pathways of exposure.” “Sentinel exposure” needs to be included **as part of** assessing aggregate exposure—these should not be considered mutually exclusive and EPA should not choose to incorporate one or the other. Instead, we recommend that sentinel exposure be considered within the context of aggregate exposure when appropriate. Under the definition of pathways of exposure, EPA should add ‘dust’ as one of the modes by which people are exposed, in addition to food, water, soil, and air. Recent research underscores that dust is a very important pathway of exposure, especially for children.<sup>4</sup>

**4. Improve the clarity and scientific basis of EPA’s description of “factors (considered) in determining unreasonable risk.” While we support that EPA’s decision to not codify a definition for “unreasonable risk,” we strongly support characterizing cancer and non-cancer “hazard” and not “risk” in these factors.**

While we support that EPA’s decision to not codify a definition for “unreasonable risk” in the rulemaking, we also strongly recommend modification to the proposed rule’s language for “factors (considered) in determining unreasonable risk.” In particular EPA should say “characterization of cancer and non-cancer “hazard” and not “risk” – hazard is what is listed in section 2605(b)(4)(D)<sup>5</sup>. In addition, EPA needs to remove any reference to specific methods used in the list of factors, in particular “margins of exposure.” We agree EPA should incorporate a factor of characterization of cancer and non-cancer risks, but it would not be appropriate here to discuss particular methods utilized to evaluate these risks. This should be addressed in guidance documents relevant to risk evaluation. We also recommend removal of the phrase ‘irreversibility of hazard’ which includes a base assumption that adverse health effects are irreversible. EPA has regulated adverse effects that are reversible and constitute a public health risk (e.g., ozone exposures).

These changes are in keeping with the statute, which identifies the minimum components EPA must include in all chemical substance risk evaluations: the scope of the risk evaluation that will be conducted, and that includes the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations the EPA expects to consider.<sup>5</sup>

*Current language in the proposed rulemaking* – “In general, EPA may weigh a variety of factors in determining unreasonable risk. These factors include, but are not limited to, characterization of cancer and non-cancer risks (including margins of exposure for non-cancer risks), the population exposed (including any susceptible populations), the severity of hazard (the nature of the hazard), the irreversibility of hazard, uncertainties, and estimates of cumulative exposure.”

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<sup>3</sup> National Research Council. Committee on the Health Risks of Phthalates, Board on Environmental Studies and Toxicology, Division on Earth and Life Studies. 2008. Phthalates and cumulative risk assessment: the task ahead. Washington, D.C.: National Academies Press.

<sup>4</sup> Mitro SD, Dodson RE, Singla V, Adamkiewicz G, Elmi AF, Tilly MK, Zota AR. 2016. Consumer product chemicals in indoor dust: a quantitative meta-analysis of US studies. Environmental science & technology. 50(19):10661-72.

<sup>5</sup> 15 U.S.C. § 2605(b)(4)(D)

*Our recommended replacement language* – “In general, EPA may weigh a variety of factors in determining unreasonable risk. These factors include, but are not limited to, characterization of cancer and non-cancer hazards, the population exposed (including any susceptible populations), the severity of hazard (the nature of the hazard), uncertainties, and estimates of cumulative exposure.”

**5. Use health-protective default values to reflect and account for the range of variability and susceptibility anticipated in the population.**

We strongly support the use of health protective defaults to incorporate factors that reflect the range of variability and susceptibility in the population to ensure risks are not underestimated. The importance of using protective science-based defaults was recommended by the NAS in 2009.<sup>2</sup> Newer science demonstrates that EPA’s typical safety factor of 10 is insufficient to account for variability due to life stage, genetics, underlying disease status, and external stressors that may be due to poverty or other difficult life conditions. It has been proposed that although this susceptibility variable is distributed broadly in the human population, a factor of 25- to 50- may account for the variability between the median individual and those with more extreme responses.<sup>2</sup> For cancer, the NAS found that differences in median versus higher-end response to carcinogens differ by a factor of 25.7.<sup>2</sup>

The use of defaults is typically a component of risk assessment, as a way to handle the common issue of missing data. Historically, EPA has relied on standard default values (“uncertainty” or “safety” factors) that have been applied across the board to various chemicals and health outcomes. However, science has since evolved and there are now more scientifically-based values that can be used when specific information is missing. For example, science has shown that developmental life stages, including the fetus, infancy, and childhood, are more vulnerable periods of exposure to chemicals. However, typical EPA age-dependent adjustment factors account for other life stages but NOT fetal exposures. This is a critical point to address, as fetal development is the most sensitive time period of one’s life and has implications for healthy development and outcomes that can persist into adulthood. EPA should evaluate this rich body of literature to identify the most up-to-date scientific knowledge regarding human variability and susceptibility and incorporate these scientifically-based default values in their assessments when specific data are lacking. For example, the California EPA has developed child-specific risk values for chemicals (i.e., atrazine, chlorpyrifos, lead, nickel, manganese, heptachlor, etc.) that specifically address child-specific routes of exposure and differences in children’s susceptibility compared to adults. EPA should review this body of evidence and incorporate these values as appropriate.<sup>6</sup> Furthermore, a default guidance principle should be that animal findings are relevant to humans unless there is sufficient and compelling information to support otherwise.

**6. Incorporate the knowledge and perspective of vulnerable populations into EPA’s risk assessment.**

EPA should incorporate the real-world experience and perspective of communities who are overburdened by pollution, environmental hazards, and social and economic stressors. These communities are exposed to a disproportionate share of pollution and subsequent adverse health impacts. These communities are often made up of people of color and lower income who are exposed to a multitude of pollution exposures that collectively increase the risk of harm, combined with synergistic

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<sup>6</sup> California Environmental Protection Agency. Office of Environmental Health Hazard Assessment (OEHHA). Child-Specific Reference Doses (chRDs) Finalized to Date. Available from: <http://oehha.ca.gov/risk-assessment/chrd/table-all-chrds>



effects with other health stressors in their daily lives such as limited access to quality health care.<sup>7</sup> EPA should incorporate guidance for their risk assessments that advance environmental justice and truly protect the health of all by reducing environmental exposures and resulting health impacts in these overburdened communities. At a minimum, this includes updating risk assessment guidelines to account for cumulative impacts of multiple exposures and underlying vulnerabilities, in particular by incorporating alternate methods to assess risk that better capture and represent those faced by overburdened and underserved communities.

## 7. Remove all language and reference to Margin of Exposure.

EPA should not use Margin of Exposure (MOE) language in the proposed rulemaking AND EPA should not use MOE as a method in the risk evaluation process.<sup>8</sup> MOE is not an estimate of risk because it does not provide information about risk at various exposure estimates. Rather, MOE is another version of the “bright line” approach similar to the Reference Dose (or Reference Concentration for inhalation doses) as it is calculated by dividing the point of departure (e.g., LOAELs, NOAELs or BMDs) by estimated exposure values. This ‘bright line’ approach does not reflect knowledge about what the potential risks are above, at or below this line. Further, it assumes that there is a “safe” level of exposure below which no harm will occur. While this may be true for a select few chemicals, the NAS recognizes that this is not a scientifically valid across the board assumption for all chemicals and has recommended moving away from such “bright line” approaches which do not establish risk estimates across the full range of exposures.<sup>2</sup> Furthermore, the EPA cannot conduct a benefits analysis using solely the MOE because there is no accompanying dose-response information, and will therefore underestimate the risks for noncancer health effects

As it is not scientifically accurate to represent MOE as an estimate of risk we recommend that EPA utilize available analytical methods to develop quantified estimates of risk that can be of use to both risk managers and decision-makers. Specifically, we recommend that EPA:

- Always use a point of departure (POD) of a benchmark dose (BMD) at 1% for calculating cancer or non-cancer risks. The POD should be based on a BMD calculation. The NOEAL/LOAEL should not be used unless the data are insufficient to model. EPA already recognizes that calculating a BMD is superior in that BMDs account for the shape of the dose–response function, are independent of study design, such as the space between dosing, and are comparable across chemicals.<sup>9</sup> There are several options for calculating non-cancer risks based on a POD. For simplicity, EPA can use the same approach as for cancer, which assumes a straight line from the POD. This is consistent with the NAS recommendation to harmonize cancer and non-cancer risk assessment, and also consistent with current science that indicates that similar perturbed biological processes can contribute to both cancer and non-cancer effects. Further, a linear relationship is in many cases likely to underestimate risks as it has been shown for several chemicals that the dose-response curve is often supra-linear.

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<sup>7</sup> Morello-Frosch R, Zuk M, Jerrett M, Shamasunder B, Kyle AD. 2011. Understanding the cumulative impacts of inequalities in environmental health: implications for policy. *Health affairs*. 30(5):879-87.

<sup>8</sup> According to EPA: Margin of exposure (MOE), which is the magnitude by which the NOAEL of the critical toxic effect exceeds the estimated exposure dose (EED), where both are expressed in the same units:  $MOE = NOAEL \text{ (experimental dose)} / EED \text{ (human dose)}$ . When the MOE is equal to or greater than  $UF \times MF$ , the need for regulatory concern is likely to be small. (<https://www.epa.gov/iris/reference-dose-rfd-description-and-use-health-risk-assessments> - Reference Dose (RfD): Description and Use in Health Risk Assessments, Background Document 1 March 15, 1993

<sup>9</sup> Wignall JA, Shapiro AJ, Wright FA, Woodruff TJ, Chiu WA, Guyton KZ, Rusyn I. 2014. Standardizing benchmark dose calculations to improve science-based decisions in human health assessments. *Environmental health perspectives*. 122(5).

- Calculate risks for cancer (and non-cancer when using the cancer method approach) using a default factor of 26 to account for human variability in the population. As described above in Comment 5, newer science demonstrates that EPA’s typical safety factor of 10 is insufficient to account for variability due to life stage, genetics, underlying disease status, and external stressors that may be due to poverty or other difficult life conditions. Other methods have also been proposed which EPA can use including probabilistic methods, such as the use of probability distributions for variables to characterize uncertainty and variability quantitatively. This modeling provides the ability to identify and characterize exposure distributions for sensitive and at risk groups in addition to better accounting for the uncertainty surrounding the data and natural variability among the population.

**8. DO NOT codify the weight of evidence (WOE) process but DO clarify the definition of the term WOE in the background section.**

We strongly support that EPA’s choice to not codify the WOE process or the approaches to using it. We strongly agree with the statement that “Codifying a specific definition can inhibit the flexibility of the Agency to quickly adopt and implement changing science.” However, to serve as guidance, we recommend that EPA clarify in the Background language the relationship between WOE and systematic review. In particular, systematic review methodology includes developing a protocol for the assessment, identifying evidence, evaluating studies, integrating the evidence, and making systematic and transparent conclusions about the strength of the scientific evidence related to the health hazards of exposure to environmental chemicals. We also recommend that as part of the evidence evaluation that conflict of interest (in particular, financial conflicts of interest) be incorporated as part of the evidence evaluation. EPA should also include the Congressional report language that defines WOE in the Background section of the FR, (but as above not in the Final Rule) which is as follows:

*“The term “weight of evidence” refers to a systematic review method 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. This requirement is not intended to prevent the Agency from considering academic studies, or any other category of study. The Committee expects that when EPA makes a weight of the evidence decision it will fully describe its use and methods.”*

EPA’s discussion of WOE should also include a reference to the National Academy of Sciences 2014 report *Review of EPA’s Integrated Risk Information System (IRIS) Process*, and clearly state that there is no uniform agreement about the utility of the term WOE, as the NAS clearly states that “the phrase *weight of evidence* has become far too vague as used.”<sup>10</sup>

Further, we agree with EPA’s statement that WOE “...is not a simple tallying of the number of positive and negative studies”. Systematic review methods applicable for environmental health have been developed through both the National Toxicology Program’s Office of Health Assessment and Translation (OHAT)<sup>11,12</sup> and the Navigation Guide methodology<sup>13,14</sup>. OHAT has also published a

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<sup>10</sup> National Research Council. Committee to Review the IRIS Process, Board on Environmental Studies and Toxicology, Division on Earth and Life Studies. 2014. *Review of EPA’s Integrated Risk Information System (IRIS) Process*. National Academies Press: Washington, DC.

<sup>11</sup> National Institute of Environmental Health Sciences (NIEHS). National Toxicology Program (NTP). Office of Health Assessment and Translation (OHAT). OHAT Systematic Review. Available from: <https://ntp.niehs.nih.gov/pubhealth/hat/noms/index-2.html>

<sup>12</sup> Rooney AA, Boyles AL, Wolfe MS, Bucher JR, Thayer KA. 2014. Systematic review and evidence integration for literature-based environmental health science assessments. *Environmental Health Perspectives (Online)*. 122(7):711.

<sup>13</sup> University of California, San Francisco. Program on Reproductive Health and the Environment. Navigation Guide Systematic Review Methodology. Available from: <http://prhe.ucsf.edu/navigation-guide>

handbook outlining specifically how to conduct a robust review with examples.<sup>15</sup> Further, case studies using the Navigation Guide method published in the literature demonstrate that systematic reviews are critical improvements over expert-based narrative reviews.<sup>16,17</sup> The application of systematic and transparent methods in hazard and risk assessment will increase the transparency and robustness of EPA's findings. We recommend that EPA refer to these methods specifically in its Background on WOE as exemplary of systematic review methods, similar to the language used in the 2014 Review of IRIS NAS report as "...an approach that would substantially strengthen" EPA chemical assessments.<sup>10</sup>

We do not agree with the following statement written in the background section:

"EPA believes the proposed risk evaluation process generally reflects the use of systematic review approaches that are appropriate for the types and quantity of information used in a chemical risk evaluation."

The NAS as recommended systematic review methods as "...an approach that would substantially strengthen" EPA chemical assessments.<sup>10</sup> As we have noted in previous comments to EPA on their risk assessments under TSCA that their current approaches to not use all the recommended elements of a systematic review – including development of a protocol beforehand that includes a PECO statement based on the study question, establishing clear inclusion/exclusion criteria, conducting a thorough and transparent literature search to identify evidence, evaluate risk of bias (or internal validity) for each included study, evaluate the quality and strength of the overall body of evidence, integrating the evidence, and making systematic and transparent conclusions about the strength of the evidence related to the human health hazards of exposure in the population.

## 9. Do not conflate hazard assessment with risk assessment.

While we agree with the general scope of the hazard assessment section, EPA should delete the language that states, "*The hazard assessment will consider the dose or concentration and resulting effect or response.*" This sentence is not consistent with EPA guidance and NAS reports.<sup>2</sup> For instance, in the EPA's Guidelines for Carcinogen Risk Assessment, hazard assessment is described as a process "to review and evaluate data pertinent to two questions: (1) whether an agent may pose a carcinogenic hazard to human beings, and (2) under what circumstances an identified hazard may be expressed."<sup>18</sup> Long-standing risk assessment practice dictates that evaluating a hazard is to be separated from the dose-response/calculation of risk. Further, exposures should not be considered in the hazard assessment phase but rather should be evaluated when looking at risk management strategies.

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<sup>14</sup> Woodruff TJ, Sutton P. 2011. An evidence-based medicine methodology to bridge the gap between clinical and environmental health sciences. *Health Affairs*. 30(5):931-7.

<sup>15</sup> National Institute of Environmental Health Sciences (NIEHS). National Toxicology Program (NTP). Office of Health Assessment and Translation (OHAT). 2015. Handbook for Conducting a Literature-Based Health Assessment using OHAT Approach for Systematic Review and Evidence Integration. Available from: [https://ntp.niehs.nih.gov/ntp/ohat/pubs/handbookjan2015\\_508.pdf](https://ntp.niehs.nih.gov/ntp/ohat/pubs/handbookjan2015_508.pdf)

<sup>16</sup> Johnson PI, Sutton P, Atchley DS, Koustas E, Lam J, Sen S, Robinson KA, Axelrad DA, Woodruff TJ. 2014. The Navigation Guide—evidence-based medicine meets environmental health: systematic review of human evidence for PFOA effects on fetal growth. *Environmental Health Perspectives*. 122(10).

<sup>17</sup> Lam, J., Koustas, E., Sutton, P., Johnson, P.I., Atchley, D.S., Sen, S., Robinson, K.A., Axelrad, D.A. and Woodruff, T.J. 2014. The Navigation Guide--Evidence-Based Medicine Meets Environmental Health: Integration of Animal and Human Evidence for PFOA Effects on Fetal Growth. *Environmental Health Perspectives*, 122(10), p.1040.

<sup>18</sup> U.S. Environmental Protection Agency (EPA). 2005. Guidelines for Carcinogen Risk Assessment. EPA/630/P-03/001B. Available from: [https://www3.epa.gov/airtoxics/cancer\\_guidelines\\_final\\_3-25-05.pdf](https://www3.epa.gov/airtoxics/cancer_guidelines_final_3-25-05.pdf)

## **10. Increase transparency.**

EPA specifically requested comment on whether and how the proposed rule could provide additional transparency, public accountability, and opportunities for public participation. As above, we recommend more use of systematic review to support transparency. We also support public comment periods that allow for adequate time for participation from a wide range of stakeholder groups. Critically important, EPA’s science advisory committees should also be open to members of the public from affected communities or those working in occupation settings to increase accountability and to take into consideration feedback from individuals who are directly impacted by chemical exposures and the decisions made under TSCA implementation.

We also strongly support the proposed language in the rulemaking that specifies that the rulemaking codify the description of the process and that it not include ‘highly detailed provisions’ to ensure that EPA can be responsive to “advancement of the science of risk evaluation and the science and technology that inform risk evaluation”. Further, we support language that clarifies that EPA will make the decision-making process transparent and accessible.

We agree that EPA needs to conduct a peer review of the risk assessments. EPA should oversee and respond to all relevant peer review comments as this is an inherently governmental function.

The term “fit for purpose” appears in the preamble. This term is too vague and EPA needs to be transparent about the data and assumptions they use to come to their conclusions. EPA should not use “fit for purpose” to justify poor risk evaluation decisions. For example, data that support low risk or low exposures should not be a cause for exclusion—these need to be incorporated into aggregate risk considerations.

## **11. Do not equate Good Laboratory Practice (GLP) with study quality.**

EPA should not include GLP or OECD guidelines studies as an example of complying with study quality. GLP alone is not an appropriate measure of study quality and does not guarantee study quality. In practice, GLP methods often do not use most current scientific methods. Moreover, GLP methods can have study design flaws that limit their ability to assess low-dose exposures, endocrine disrupting effects, behavioral or learning deficits, and upstream perturbations. GLP studies are also not consistently associated with higher quality research, proper study design, or correct statistical analysis.<sup>19,20,21</sup> Further, GLP studies are often sponsored by industry and thus can be biased due to financial conflict of interest.<sup>22,23</sup> We recommend that EPA delete mention of GLP from its rule so as to not perpetuate a false equation of GLP and study quality.

## **12. Correct an error in stakeholder feedback section.**

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<sup>19</sup> Krauth D, Woodruff TJ, Bero L. 2013. Instruments for assessing risk of bias and other methodological criteria of published animal studies: a systematic review. *Environmental Health Perspectives*. 121(9).

<sup>20</sup> Myers JP, vom Saal FS, Akingbemi BT, Arizono K, Beicher S, Colborn T, Chahoud I, Crain DA, Farabollini F, Guillette Jr LJ, Hassold T. 2009. Why public health agencies cannot depend on good laboratory practices as a criterion for selecting data: the case of bisphenol A. *Environmental Health Perspectives*. 117(3):309.

<sup>21</sup> Cornwall, Warren. 2017. Rules of evidence. *Science*. 355(6325):564-567.

<sup>22</sup> Rennie D. 2010. Integrity in scientific publishing. *Health Serv Res* 45:885–896.

<sup>23</sup> Lexchin J, Bero LA, Djulbegovic B, Clark O. 2003. Pharmaceutical industry sponsorship and research outcome and quality: systematic review. *Bmj*. 326(7400):1167-70.

In Section II. D *Stakeholder Feedback* Third parties submitting draft risk assessments, EPA incorrectly states the following “Due to changes in the law, manufacturers are now able to submit their own draft risk evaluations.” This is incorrect--the law allows for ‘interested person’ to develop and submit draft risk assessment. This needs to be corrected as any party, including the public, is included. Relevant language is from section 26(l)(5)<sup>24</sup>:

(5) Guidance

Not later than 1 year after June 22, 2016, the Administrator shall develop guidance to assist interested persons in developing and submitting draft risk evaluations which shall be considered by the Administrator. The guidance shall, at a minimum, address the quality of the information submitted and the process to be followed in developing draft risk evaluations for consideration by the Administrator.

We are appreciative of the opportunity to provide public input and we look forward to continuing to participate in such opportunities in the near future. Please do not hesitate to contact us with any questions regarding these comments.

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<sup>24</sup> 15 U.S.C. § 2625(l)(5)