March 20, 2017

Comments from Academics, Scientists, and NGOs on the Prioritization of Chemicals for Risk Evaluation under the Toxic Substances Control Act

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Comments submitted to EPA–HQ–OPPT–2016–0636 and by email to Ryan Schmit, Immediate Office, Office of Chemical Safety and Pollution Prevention, Environmental Protection Agency, 1200 Pennsylvania Ave. NW, Washington, DC 20460–0001; telephone number: (202) 564–0610; email address: schmit.ryan@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 appreciate the opportunity to provide written comments on the Agency's proposal to establish a risk-based screening process and criteria that the U.S. Environmental Protection Agency (EPA) will use to identify chemical substances as either High-Priority Substances for risk evaluation or Low-Priority Substances for which risk evaluations are not warranted at the time. The new amendments to TSCA represent a critical opportunity for EPA to update their scientific approaches to evaluating the potential risk posed by industrial chemicals in commerce and to protect public health as required by the statute. Furthermore, EPA's decisions on prioritization will have far-reaching implications for future assessments of environmental chemicals more generally, on the federal but also state and local levels. We welcome EPA's engagement with the public on this process and would like to take this opportunity to voice our unwavering support for a prioritization process that is transparent, nonbiased, timely and designed to incorporate modern scientific principles on evaluating toxicity and integrating evidence from different evidence streams. EPA previously held a public meeting on August 10, 2016, in Washington D.C. and accepted written comments as well on the prioritization rule. Several of the undersigned submitted oral and written comments at that time. We appreciate this subsequent follow-up opportunity to submit further comments to respond to information provided by EPA on the development of its prioritization process.

In general, we strongly support EPA in its efforts to improve the evaluation of hazard assessment of chemicals through the Frank R. Lautenberg Amendments to TSCA to make them timely and health protective. Such improvements are urgently needed and long overdue and we view this as a critical opportunity for EPA to take action to reduce exposures to chemicals that are recognized as potential hazards from their designation as High-Priority Substances and the subsequent risk evaluation. We recommend the Agency continue to fulfill these statutory mandates in a timely manner while also supporting the Agency's overall duty to protect public health and prevent harmful exposures to environmental chemicals.

In fulfillment of these statutory mandates, we would like to take this opportunity to make the following comments:

1. **We agree there is no need for EPA to define terms such as "best available science," "weight of the evidence," "sufficient of information," "unreasonable risk," or "reasonably available information." Furthermore, we recommend EPA adapt systematic review methods for evaluating the scientific evidence to identify the highest quality information from which to develop prioritization determinations;**

2. **We support that EPA require "information sufficient to establish" that a chemical substance meets the definition of a Low-Priority Substance and that in the event of insufficient information at the proposed designation step, the chemical substance will by default be designated as a High-Priority Substance;**

3. **We agree with EPA's proposal to incorporate a pre-prioritization phase to, in part, evaluate the existence and availability of risk-related information on a candidate or potential candidate chemical substance for the Prioritization Process. We strongly recommend that EPA make use of its authority to require the development of necessary chemical substance toxicity information as soon as data gaps are identified to aid in the ability to prioritize and evaluate these chemicals in the future;**

4. **We recommend that EPA designate any chemical whose use in commerce results, or may result, in exposures to pregnant women and developing children as High-Priority unless there is sufficient data to show that it does not pose a risk to these and other vulnerable populations;**

5. **We recommend that EPA utilize existing knowledge presented in risk or hazard evaluations completed by EPA itself (for example, by the Integrated Risk Information System program) and other government agencies (i.e., National Toxicology Program) or authoritative bodies (i.e., the International Agency for Research on Cancer and California's Prop 65 lists) to expedite science-based prioritization.**

Below please find additional details with respect to each of these comments.

1. **We agree there is no need for EPA to define terms such as "best available science," "weight of the evidence," "sufficient of information," "unreasonable risk," or "reasonably available information." Furthermore, we recommend EPA adapt systematic review methods for evaluating the scientific evidence to identify the highest quality information from which to develop prioritization determinations.**

We agree with EPA that many of these terms are already in use within the Agency, other federal/state agencies, or in scientific fields and there is no need to define these terms in the proposed rule. Instead, we support that these terms be defined explicitly in EPA guidance documents which are available to the public. We believe this to be critical in maximizing the Agency's flexibility to apply these concepts in their evaluations, which will prove particularly important over the long-term to keep up with concurrent evolution of scientific knowledge, methods, and innovation.

However, we note that in particular, the term "weight-of-evidence" is one that the National Academies of Science (NAS) concluded to be too vague and of little scientific use, in a recent review of EPA's Integrated Risk Information System (IRIS) program.[1] Within the Lautenberg Amendments, the Agency is required to consider the "weight of scientific evidence" and we encourage that EPA consider developing publically available guidance on this process that encompasses a broad definition of how the scientific evidence is to be evaluated beyond what is typically considered for the specific term "weight-of-evidence," for instance by incorporating recommended and empirically demonstrated approaches such as systematic review methodology.

Furthermore, we also recommend that the Prioritization Process evaluation utilize only the highest quality data, which could be identified as such from a review of the available evidence undertaken using systematic review methodology, whether for exposure or health effects. We strongly recommend that EPA incorporate a systematic and transparent method to evaluate the quality of evidence for each evidence stream it considers in its review in order to transparently carry these ratings into the evidence integration step of the Prioritization Process.

2. We support that EPA require "information sufficient to establish" that a chemical substance meets the definition of a Low-Priority Substance and that in the event of insufficient information at the proposed designation step, the chemical substance will by default be designated as a High-Priority Substance;

Under the statute, EPA "shall designate a chemical substance as a low-priority substance if the Administrator concludes, based on information sufficient to establish (without consideration of costs or other non-risk factors), that such substance does not meet the standard identified in clause (i) for designating a chemical substance a high-priority substance." Further, the statute specifically requires that a Low-Priority Substance designation be based on "information sufficient to establish" that a chemical substance meets the definition. Accordingly, we strongly support that EPA require strong, affirmative data to conclude that a chemical does NOT pose an "unreasonable" risk, as the health and associated economic consequences of being wrong --- i.e., thinking a chemical does not pose a risk when in fact it does pose a risk--are very high.

Specifically, chemicals undergoing the Prioritization process that do not yet have enough evidence to make a conclusion about their toxicity or with "unknown" toxicity should not be designated as a Low-Priority Substance. This is further supported by the Agency's interpretation of a Low-Priority Substance in its FR notice as that "…it gives the public notice of chemical substances for which potential risks are likely low or nonexistent…" In order for this interpretation to hold true, the Agency must ensure that chemicals are designated Low-Priority Substances only when there exists strong, affirmative scientific evidence of low or nonexistent toxicity to humans under all conditions of use, including reasonably foreseen uses. This is also critical because designating a chemical as High-Priority Substance has the effect of progressing to the next step of risk evaluation whereas the designation as Low-Priority Substance is a final Agency action deeming that no further evaluation is warranted at the federal level and also pre-empting state and local action on the substance. Therefore, in the absence of strong, affirmative data supporting that the chemical poses no toxicity, we support the designation of chemicals as High-Priority.

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

We agree with the language in the proposed rule that EPA plans on considering a "low bar" to classify chemicals as High Priority, as again this is simply an "interim step" before obtaining more data and undertaking a rigorous evaluation of the data follows in the risk evaluation step. Similarly, we agree with the default-to-high approach in all cases where there is insufficient information to designate a chemical as Low Priority, for the reasons discussed previously. Furthermore, we believe this will have the additional advantage in creating an incentive for companies and manufacturers to generate and provide data to EPA on these chemicals.

This is also consistent with modern science based decision-making in clinical sciences, where decisions reflect the extent to which we can be confident that desirable effects of an intervention outweigh its undesirable effects for an individual. This approach is also informed by more than a half century of lessons in the regulation of toxic chemicals, including (1) exposure to toxic chemicals increase over time, for example, from workers to consumer to future generations; (2) the nature of harm expands over time, from one adverse endpoint to many; and (3) "safe" limits get lower over time, not higher, as the science advances.

3. **We agree with EPA's proposal to incorporate a pre-prioritization phase to, in part, evaluate the existence and availability of risk-related information on a candidate or potential candidate chemical substance for the Prioritization Process. We strongly recommend that EPA make use of its authority to require the development of necessary chemical substance toxicity information as soon as data gaps are identified to aid in the ability to prioritize and evaluate these chemicals in the future.**

Based on our experience with conducting systematic reviews, there will likely be a lot of missing data and this lack of data will constrain the Agency's ability to conduct its review for Prioritization or Risk Evaluation. It is therefore critical for EPA together with scientific stakeholders to proactively identify and take steps to address these data gaps in order to advance hazard assessment. EPA is in a position to address this problem with its authority to mandate test orders, subpoenas for information or data, and funding of studies. We encourage EPA to take advantage of this as necessary to address critical data gaps; even in the pre-prioritization phase if sufficient data are missing so that the Agency deems it not possible to move the particular chemical into the prioritization process, it would still be prudent for the Agency to use its authorities to initiate the generation of necessary data, as these tests could take months or years to develop and execute and therefore in theory could be available in the near term when the Agency revisits this particular chemical for evaluation.

The evaluation of evidence should also incorporate knowledge or defaults to ensure that risks to vulnerable populations such as children and pregnant women are considered and consequently demonstrate that risks to these groups meet the criteria defined beforehand as "sufficient" evidence for low priority.

4. **We recommend that EPA designate any chemical whose use in commerce results, or may result, in exposures to pregnant women and developing children as High-Priority unless there is sufficient data to show that it does not pose a risk to these and other vulnerable populations.**

EPA is now mandated by the Lautenberg Amendments to specifically consider and protect against risks for susceptible or vulnerable populations. Pregnant women, developing fetuses and young children

represent sensitive time periods of development where exposures to harmful contaminants can pose potential serious consequences for health outcomes and lasting consequences for brain development, cognition and behavior in children. Therefore, we believe that without strong evidence demonstrating that exposures to these vulnerable populations pose minimal risk, chemicals that result in exposures to these populations should by default be classified as High-Priority and move on to the risk evaluation step. We also strongly encourage EPA to specifically list potential concerns for pregnant women and fetal health as consideration for narrowing the field for potential candidates. Currently, EPA includes "Potentially of concern for children's health" as a concern, which by extension could apply to pregnant women and developing fetuses, but we encourage EPA to specifically include these subpopulations to ensure their consideration in evaluating these chemicals.

5. **We recommend that EPA utilize existing knowledge presented in risk or hazard evaluations completed by EPA itself (for example, by the Integrated Risk Information System program) and other government agencies (i.e., National Toxicology Program) or authoritative bodies (i.e., the International Agency for Research on Cancer and California's Prop 65 lists) to expedite science-based prioritization.**

EPA should use the highest quality evidence and information to support their findings in a way that supports timely decision-making. To accomplish this, EPA should leverage existing data sources by seeking knowledge about specific chemicals or analogues that have already been documented in risk or hazard evaluations completed by EPA, other government agencies (such as the National Toxicology Program or the California Environmental Protection Agency), or other authoritative body (International Agency for Research on Cancer) to extrapolate findings to the chemical under review when appropriate. These assessments provide useful data and information on hazard of chemicals as well as evidence summaries and integration of existing data and can provide a critical immediate source of data on recognized hazards or estimates of risk. Other federal agencies such as the Occupational Safety and Health Agency (OSHA) and the National Institute of Occupational Health Safety (NIOSH) may have additional information on exposures to these chemicals in the workplace, including medical surveillance data that may be of use. Lastly, EPA should take advantage of their authority to require data from chemical manufacturers, processors, distributors, and recyclers or issue test orders to obtain data that are understood to be lacking and also make concerted efforts to confirm the accuracy or reported data and information.

We are very appreciative for the opportunity to provide public input and we are looking 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.

Respectfully,

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