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Gina McCarthy, Administrator
U.S. Environmental Protection Agency

Jim Jones, Assistant Administrator
Office of Chemical Safety and Pollution Prevention
U.S. Environmental Protection Agency

Re: Docket Number EPA-HQ-OPPT-2016-0400

The following comments are submitted on behalf of the Environmental Working Group (EWG), a nonprofit environmental health advocacy organization. EWG has spent over a decade advocating for reforms to strengthen the Toxic Substances Control Act (TSCA). Deficiencies in Section 6 that stymied efforts to enact health-protective regulations for existing chemicals were a frequent target of those reform efforts. Many of EWG's concerns related to Section 6 were not addressed in the Frank R. Lautenberg Chemical Safety for the 21st Century Act. Nonetheless, we recognize the unprecedented opportunity presented by the new requirement that the Environmental Protection Agency (EPA) finally systematically review existing chemicals under its Section 6 authority. EPA should use its expanded authority to create a robust, data-driven risk evaluation process that will give it a full picture of a chemical's risks to the environment and people, including particularly vulnerable populations like children or people residing in fenceline communities.

As such, we offer the following comments:

1. **Use of order authority to fill data gaps**

EPA must ensure that it has adequate data when conducting risk evaluations. To that effect, EPA should use its expanded authority to order new testing data during risk evaluations, and should know what kind of data it needs before it even begins a risk evaluation.[1] Such authority should be used in a timely manner to speed up information collection and provide those that manufacture, process and dispose of chemicals with adequate time to produce the data.

The experience of regulators in Europe is instructive. In a 2002 report on the first 41 completed risk assessments of existing chemicals under the Existing Substance Regulation 793/93, the European Chemicals Bureau highlighted the need to fill data gaps early in the review process.[2] Their evaluation concluded, "[O]ur a priori knowledge of possible risks of priority chemicals is found to be poor, especially for consumers." The lack of safety testing data and the poor information, along with the high number of unforeseen uses of chemicals, seriously hindered efforts to protect public health in a timely manner. Additional data on chemical toxicity and use changed regulators' assessments of expected risks to consumers, workers and the environment.

This experience, in part, likely led European regulators to take a more data-driven approach under Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH).

The need to request data early to fill gaps is also exemplified by some of EPA's current scoping documents and problem formulations. For example, EPA must request additional information on toxicity and exposure to chemicals included in the chlorinated phosphate esters flame retardant cluster to revise and strengthen its initial problem formulation. EPA identified dermal and inhalation routes as potential exposure sources for both workers and consumers, but did not include risk evaluation of these routes in its initial assessment.[3] EPA stated that "EPA/OPPT expects industrial worker exposures to be primarily via inhalation of vapor and dermal contact; given the lack of toxicity data for inhalation and dermal routes of exposure, these exposure pathways cannot be quantified in a risk assessment,"[4] and that the potential for consumer inhalation and dermal contact exposure is high. Without ordering any information on worker or consumer exposures via these routes, EPA will not be able fulfill its mandate to ensure the chemicals pose no risk.

EPA may utilize its order authority to request additional data generated by validated high-throughput technology to generate an array of screening-level information for data-poor chemicals. Validated screening techniques may assist in closing data gaps for a spectrum of endpoints, deciding whether to consider related chemicals as a group, and identifying new areas of potential concern where additional testing may be warranted. Invertebrate and lower vertebrate assays such those using C. elegans (nematode) and D. rerio (zebrafish) may also provide important developmental and other toxicity information. According to oral comments provided during the Aug. 10 public meeting, these assays have been useful in predicting developmental and neurotoxicity for state regulatory agencies such as California EPA.[5] Other animal testing data using higher vertebrates should be minimized, but ordered where appropriate.

2. Assessing aggregate and cumulative exposures

EPA must have procedures in place to evaluate risks from all potential pathways of exposure. As part of a risk assessment, EPA is required to describe whether aggregate or sentinel exposures to a chemical substance under the conditions of use were considered.[6] Considering the *aggregate* exposures will provide a more robust analysis of the total risk a chemical poses. To properly assess aggregate exposures, EPA must consider exposures from all routes, including those not regulated by TSCA. This includes exposures from food, pesticides, and cosmetics, even if those uses are not ultimately regulated following a risk assessment. All relevant route-specific information should be incorporated into aggregate exposure assessments, and EPA should use order authority to fill identified data gaps.

Evaluation of sentinel exposure should not replace aggregate exposure assessment. Sentinel exposure evaluation and risk reduction operate under an assumption that reducing exposure in highly exposed populations would result in reductions in risk to less exposed populations. This is not an acceptable shortcut for evaluating real world exposures. It incorrectly assumes that risk assessors will always be able to determine the most highly exposed group. It also disregards the significant body of evidence that hormone disruptors and developmental toxicants may cause adverse effects at very low doses, and ignores the possibility of nonmonotonic dose-response

curves. The pharmaceutical literature is rife with examples of nonmonotonicity, timing and age-group specific toxicity concerns. One key example is the pharmaceutical administration of DES to pregnant women, which posed the most serious risks to developing fetuses.

Although cumulative exposures are not required to be part of a risk assessment under the law, EPA is explicitly permitted to order testing and prescribe protocols and methodologies for a number of health and environmental effects – including "cumulative or synergistic effects."[7] EPA should use this authority and consider such cumulative exposures to the extent practicable to achieve a fuller understanding of the potential risks. This includes exposures that may affect similar biological pathways and exert additive or synergistic effects. EPA may consider collective exposure to groups of similar chemicals, and use the Adverse Outcome Pathway framework and database[8] to identify where cumulative effects may be an issue.

Cumulative exposure considerations would also improve current assessments. Public comments[9] submitted to EPA on its chlorinated phosphate ester flame retardant cluster initial assessment raised the issue that these compounds need to be assessed for neurotoxicity. The relatively sparse existing data shows concerns for neurological effects, and the structural similarity to organophosphate pesticides raises warning signs for the chemicals' effects on neurodevelopment due to inhibition of acetylcholinesterase, the mechanism of action for OPs.

3. Transparency and systematic review

Systematic review of safety information should align with National Toxicology Program's Office of Health Assessment and Translation (OHAT) guidelines,[10] and the "Navigation Guide" approach developed by the University of California San Francisco.[11] The process should be transparent, and EPA should clearly publish the criteria and guidelines used for each problem formulation and risk assessment. Failure to meet all criteria should not necessarily result in the automatic exclusion of a particular study, but it may influence how the study is weighted in an assessment. If studies are excluded from consideration, the rationale should be transparent to the public. Studies that do not meet good laboratory practices standards or test guidelines such as OECD should not be automatically be excluded.

4. Assessments by chemical groupings

EPA is explicitly allowed to group chemicals by category under Sec. 26(c).[12] Reviewing groups or categories of chemicals may be a way for EPA to more quickly and efficiently assess the more than 1,000 chemicals that it has identified as likely needing review.[13] EPA's previous framework included groupings of chemicals for combined assessment or regulatory action plans, such as the chlorinated phosphate ester flame retardant cluster and the group of eight phthalates.[14] While each chemical in a grouping must be considered individually for unique properties, chemical grouping is a reasonable approach for risk assessment and may help in the evaluation of cumulative exposure, or avert the substitution of one harmful chemical with a closely related replacement. EPA should determine whether poorly studied group members can be considered to have additive and cumulative risks to other group members.

In terms of EPA's effort to meet the required timeframe for chemical assessments, we recommend that each group collectively count as one Work Plan chemical assessment. For example, EPA's requirement to publish a list of 10 Work Plan chemicals,[15] for which to initiate risk evaluations within 180 days, should not be fulfilled by evaluating all eight phthalates from the Phthalates Action Plan and two other chemicals. If chosen, the group of eight phthalates – or however many are chosen for a new phthalates group – should count as one assessment.

5. **Unique exposure considerations and vulnerable populations**

The risk assessment process must consider any unique risks to different populations – such as workers, consumers, children, etc. – at each point in the life cycle of a chemical. As part of this consideration, EPA should consider potential health and environmental risks for communities near places where chemicals are produced, processed, stored or disposed of – whether or not they are close to drinking water sources. This includes fenceline communities that may be disproportionately impacted by environmental releases, and children who may have carry-home exposures from occupationally exposed parents. EPA should also consider unique exposures that may be due to cultural or ethnic practices, such as subsistence diets, in its risk assessments.

In addition to the life cycle of the chemical, life stage-specific vulnerabilities should be identified where possible for both those in early stages of development and the aging, as well as potential in-utero exposures. EPA should also consider the immunocompromised, genetic polymorphisms, disease burdens, and effects of common pharmaceuticals which could confer susceptibility to adverse health effects.

6. **Use of CBI in risk assessments**

EPA should offer more transparency for data reporting claimed as confidential business information (CBI). For example, in EPA's problem formulation and initial assessment of 1,4 dioxane, the most recent chemical reporting data for 2012 was claimed CBI.[16] EPA should report general information describing aggregate production and import volumes of chemicals under assessment to give stakeholders a fuller picture of how pervasively a chemical is used.[17]

Additionally, EPA should always disclose chemical identity in health and safety studies used as part of chemical risk assessments, to the extent that identity does not disclose manufacturing processes or the portion of a chemical used in a particular mixture.[18] Although EPA was not prohibited from disclosing chemical identity from health and safety studies prior to the Lautenberg amendments to TSCA, it often elected not to do so and protected the studies as CBI. For example, one Section 8(e) submission from February 2016 reported that an unnamed chemical from an unnamed company caused decreased fertility and changes in the lungs, spleen, stomach, intestines and vagina. The test substance also killed half the rats in experiments that exposed them to 100 mg/kg/day and then 80mg/kg/day.[19] Protecting this information as a trade secret deprives the public of valuable data about a chemical's safety, and makes it much more difficult for the public to evaluate the rigor and adequacy of EPA's risk evaluations.

7. **Population-based risk estimates for non-cancer endpoints**

EPA should incorporate the National Academy of Sciences' recommendations for population-based risk estimates in their risk assessments as standard practice, as described in *Science and Decisions: Advancing Risk Assessment*.[20] This will improve assessments by providing an actual estimation of risk, instead of limiting assessments to a Margin of Exposure (MOE) approach that gives no population-based risk estimation and simply serves as a cutpoint. Careful study of the non-cancer toxicities of chemicals like mercury, lead and arsenic increasingly reject the concept of a toxicological threshold below which there is no chance of harm. Instead, EPA should assume chemicals follow a probability of adverse effects at low levels of exposure and use tools which provide more robust assessment of data from studies of non-cancer effects.[21]

8. Reasonably foreseen conditions of use

The amended version of TSCA defines "conditions of use" as "the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of."[22] As such, EPA should consider not only the intended and known conditions of use, but also reasonably foreseeable conditions of use during problem formulations and risk assessments. Unintended uses can lead to increased exposures that should be considered when evaluating safety. For example, scientists only recently discovered and reported that gymnasts had higher than expected exposures to chemical flame retardants, which they traced to the widespread use of flame retardants in polyurethane foam used in landing pads and foam pits.[23,24] To the extent that gyms were sold waste scraps of polyurethane foam treated to pass furniture flammability standards, one could argue that gymnasts' exposures were not based on the intended conditions of use. But we argue against this narrow definition because such use is foreseeable. Furthermore, uncommon but intense exposures due to off-label product use or accidents should be included since both occur with regularity. Finally, risk evaluations should not be limited to individual uses of a chemical, but should encompass all conditions of use and likely exposures.

9. Procedural rule

Finally, we emphasize that the law requires EPA to propose and finalize a rule to establish a *process* for risk evaluation.[25] EPA's proposed rule should establish a framework for risk evaluation but need not delve deeply into detail on the scientific methodologies and information requirements. EWG recognizes that different chemical assessments may require different approaches and different kinds of information. More detailed information can and should be provided in the EPA guidance and policy documents required under Section 26(l). This approach lessens the administrative burden on EPA and provides it more flexibility to craft a risk evaluation that fits the specific profile of a particular chemical. These documents are also more flexible, and EPA may change them more easily in the future as best practices and technologies evolve.

Thank you for considering the comments above. EWG looks forward to other opportunities to comment on TSCA implementation and work with EPA toward more rigorous regulation of toxic chemicals in commerce.

Sincerely,

Johanna Congleton, MSPH, Ph.D.
Senior Scientist

David Andrews, Ph.D.
Senior Scientist

Melanie Benesh, J.D.
Legislative Attorney

Sonya Lunder, MSPH
Senior Analyst

[1] 15 U.S.C. § 2603(a)(2)(A)(1)(i).
[2] C.W.M. Bodar et al., RIVM report 601504002/2002, Evaluation of EU Risk Assessments Existing Chemicals (EC Regulation 793/93) (2002), http://www.rmri.ro/EU_2850/Downloads/RIVM_report_601504002.pdf.
[3] Envtl. Prot. Agency, Office of Chemical Safety & Pollution Prevention, TSCA Work Plan Chemical Problem Formulation & Initial Assessment: Chlorinated Phosphate Ester Cluster Flame Retardants (Aug. 2015), https://www.epa.gov/sites/production/files/2015-09/documents/cpe_fr_cluster_problem_formulation.pdf.
[4] Id.
[5] Gina Solomon, Deputy Sec'y for Health & Sci. at Cal. Envtl. Prot. Agency, Oral Comment at EPA Public Meeting on Section 6 Prioritization (Aug. 10, 2016).
[6] 15 U.S.C. § 2605(b)(4)(F)(ii).
[7] 15 U.S.C. § 2603(b)(2)(A).
[8] Adverse Outcome Pathway Knowledge Database, http://aopkb.org/ (last visited Aug. 17, 2016).
[9] Earthjustice, Nat'l Res. Def. Council, Wash. Toxics Coal., Comment Letter on Problem Formulation and Data Needs Assessment for the Brominated Phthalates Flame Retardant Cluster (Jan. 20, 2016), https://www.regulations.gov/document?D=EPA-HQ-OPPT-2015-0068-0027.
[10] Nat'l Toxicology Program, OHAT Systematic Review, https://ntp.niehs.nih.gov/pubhealth/hat/noms/index-2.html (last visited Aug. 17, 2016).
[11] Tracey J. Woodruff, Patrice Sutton, & The Navigation Guide Work Grp., An Evidence-Based Medicine Methodology to Bridge the Gap Between Clinical & Envtl. Health Sci., 35 Health Affairs 931(2011), http://content.healthaffairs.org/content/30/5/931.full.pdf+html?ijkey=z58MCEPW2X49.&keytype=ref&siteid=healthaff.
[12] 15 U.S.C. § 2625(c).
[13] Jim Jones, Assistant Admn'r, EPA Office of Chemical Safety & Pollution Prevention, Testimony before Senate Comm. on Env't & Pub. Works (Mar. 18, 2015), http://www.epw.senate.gov/public/_cache/files/6072fb1c-06a0-48b5-9dd4-2d894a81e9c0/spw031815.pdf.
[14] Envtl. Prot. Agency, Assessments for TSCA Work Plan Chemicals, https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/assessments-tsca-work-plan-chemicals (last visited Aug. 23, 2016).
[14] 15 U.S.C. § 2605(b)(2)(A).
[15] 15 U.S.C. § 2605(b)(2)(A).
[16] Envtl. Prot. Agency, Office of Chemical Safety & Pollution Prevention, EPA Document# 740-R1-5003, TSCA Work Plan Chemical Problem Formulation and Initial Assessment: 1,4-Dioxane (Apr. 2015).
[17] This kind of general information is not protected from disclosure under section 14(b)(3). 15 U.S.C. § 2613(b)(3).
[18] See 15 U.S.C. § 2613(b)(2). Because this section merely does not prohibit EPA from disclosing this information, companies may still claim chemical identity as CBI. EPA should reject most of these claims.
[19] Letter from [ ], to Envtl. Prot. Agency, Re: [ ]; TSCA Section 8(e) Submission for Substance with TSCA Confidential Inventory Accession Number 8692 (Feb. 17, 2016), java.epa.gov/oppt_chemical_search/proxy?filename=090225268024381f_8EHQ-16-20276_368174.pdf.
[20] Nat'l Acad. of Sci., Science & Decisions: Advancing Risk Assessments (2009), http://www.nap.edu/catalog/12209/science-and-decisions-advancing-risk-assessment.
[21] Salomon Sand et al., The Current State of Knowledge on the Use of the Benchmark Dose Concept in Risk Assessment, 28 J. of Applied Toxicology 405 (2008), http://onlinelibrary.wiley.com/doi/10.1002/jat.1298/full.
[22] 15 U.S.C. § 2602(4).

[23] Courtney C. Carignan, Mingliang Fang, Heather M. Stapleton, Wendy Heiger-Bernays, Michael D. McClean, & Thomas F. Webster, Urinary Biomarkers of Flame Retardant Exposure Among Collegiate U.S. Gymnasts, 94 Env't Int'l 362 (2016).
[24] Courtney C. Carignan, Wendy Heiger-Bernays, Michael D. McClean, Simon C. Roberts, Heather M. Stapleton, Andreas Sjödin, & Thomas F. Webster, Flame Retardant Exposure Among Collegiate United States Gymnasts, 47 Envtl. Sci. & Tech. 13848 (2013).
[25] 15 U.S.C. § 2605(b)(4)(B) (emphasis added).