NATURAL RESOURCES DEFENSE COUNCIL

Comments from the Natural Resources Defense Council

Risk-Based Procedural Rule for Chemical Prioritization under TSCA
as amended by the Frank R. Lautenberg Chemical Safety for the 21st Century Act

Docket EPA-HQ-OPPT-2016-0399

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The Natural Resources Defense Council ("NRDC") is a national, non-profit environmental organization of lawyers, scientists, and other professionals. NRDC presents these comments on behalf of our 1.4 million members and online activists. NRDC does not have any financial interest in the topic of these comments.

Under the newly amended Toxic Substances and Control Act, EPA has been mandated to promulgate a final rule that establishes a screening process including criteria for designating chemical substances as high-priority substances or low-priority substances -- to prioritize chemical substances or categories of chemical substances for further risk evaluation. The process for designating the priority of chemical substances, must include consideration of hazard and exposure information, and must, at a minimum, take into account potentially exposed or susceptible populations, persistence and bioaccumulation, storage near significant sources of drinking water, conditions of use, production and processing volume, and changes in these categories for chemical substances and categories of chemical substances.

In establishing a procedural rule, NRDC recommends that the Agency refrain from explicitly defining the specific protocol that will be used for prioritization decisions (e.g., a two-step process involving a numerical scoring system). We, instead, recommend that the Agency use this rulemaking to set guidelines for the procedural steps that will be taken when prioritizing chemicals and use future guidance documents to establish specific methodologies and tools for prioritization.

To aid in the development of the procedural rules under this rulemaking, our comments will focus primarily on our recommendations for the procedural steps necessary to ensure public participation and input in the prioritization process. We will then focus on recommendations for methodological requirements that should be included in future guidance documents or other arenas in which prioritization methods are discussed. These comments and recommendations ultimately seek to assist the Agency in fully upholding the law and fulfilling its mission to “protect human health and the environment”.

Procedural Steps Necessary to Ensure Public Health and Ecosystem Protection Under the Prioritization Procedural Rule.

The process of prioritizing chemicals for risk evaluation will take many years, as EPA gathers data about substances and chemicals that are designated "high priority" for the commencement of risk evaluation (or, in some instances, designated as "low priority" where EPA has sufficient information to demonstrate that a chemical cannot pose an unreasonable risk). The agency will ultimately need to "meter" the number of chemicals it chooses to designate as "high priority" (beyond the minimum number required under the law) to ensure it is not over-burdened. Metering the number of chemicals EPA works on is the proper approach to prioritization, not narrowly defining what may qualify as a "high priority" substance. EPA should use its authority, particularly under Sections 4 and 8, to obtain the information necessary, including regarding toxicity, exposure and use, prior to making a high priority designation, to ensure an informed and health protective risk evaluation is possible for "high priority" chemicals.

To ensure that the prioritization process used by the Agency under the amended TSCA is fully protective of public health, particularly of the health of vulnerable and susceptible subpopulations (including infants, children, pregnant women, workers, disproportionately exposed communities), EPA must ensure that the process is broad, inclusive, and precautionary in nature.

1. **In designing a prioritization screening protocol, EPA must adopt a prioritization screening method that is broad and ensures most chemical substances or categories of chemical substances are ultimately deemed "high priority" for risk evaluation.**

Congress established the prioritization process as the door through which chemicals must proceed prior to being evaluated, but it said little about the appropriate size of that door, other than that a chemical that "may pose an unreasonable risk to health or the environment" including to susceptible populations, because of a "potential" hazard and a "potential" exposure should be deemed high priority. The statute thus establishes a very broad scope (or, in more colloquial terms sets a very low bar) for a chemical to "qualify" as a high-priority substance. EPA, consistent with its mission to protect public health and the environment, must ensure that the prioritization step is a wide and inclusive gateway, not a narrow crevice through which few chemicals slip through.

Existing case law makes clear that the bar for EPA to establish that a chemical "may pose an unreasonable risk" to health or the environment is very low.[1] The toxicity of a chemical can be altered by a number of factors including age, co-exposures, and prior exposures. The exposure to a chemical can change drastically depending upon occupation, geographic location, and product use practices. When evaluated at the population level, even small changes in health outcomes (e.g., small decreases in IQ or small increases in body mass index) can have grave societal consequences. When identifying

[1] *Chemical Mfrs. Ass'n v. U.S. E.P.A.*, 859 F.2d, 977 (D.C. Cir. 1988); *Ausimont U.S.A., Inc. v. EPA*, 838 F.2d 93 (3rd Cir. 1988).

chemical substances that "may pose an unreasonable risk" the Agency must cast a wide net in light of the statute's bias toward protecting public health and its focus on the "potential" for harm.

Once the pool of chemical substances and categories of chemical substances has been established by the Agency, EPA must ensure that any process used to designate chemicals as "high priority" should be flexible and inclusive and take into take into account uncertainties in underlying data sources (e.g., production volume data) and variability in susceptibility (e.g., critical windows of development) and exposure (e.g., highly exposed populations like workers or disproportionately exposed communities). The Agency should use methods that are drawn from multiple data streams, that give highest weight to positive evidence of hazard, exposure, or PBT characteristics (i.e., highest score prevails rather than a normalized score), and that assumes data gaps in the areas evaluated (e.g., hazard, exposure, and PBTs) would be classified at the highest level of concern (e.g., a score of 3 under current Work Plan Methodology; EPA, 2012). The potential pool of "high priority" chemical substances and categories of chemical substances will likely be very large (although the Agency need not propose them as high priority all at once).

2. A formalized weight-of-evidence evaluation and systematic review should not be required for any prioritization process.

Prioritization is, by definition, a process that organizes tasks or things by importance. While an important step, prioritization does not imply a final decision, thus allowing flexibility in determining which task or thing is to be tackled first.

In developing a prioritization process under the amended TSCA, the Agency should develop a method that is both timely and based upon a broad array of scientific information. In order to meet both the time and public health protection requirements under the law, the Agency must create an efficient and effective process by which to assign priority classifications for chemical substances and categories of chemical substances. Weight-of-evidence approaches are judgment-based processes aimed at determining whether the evidence is strong enough to infer causality. Systematic reviews in risk assessment are information and evaluation exercises that support the integration of evidence in an assessment. Both of these processes involve extensive effort and time that, while appropriate for risk assessments, are over burdensome and unnecessary for a prioritization decision.

Endpoint Evaluation

3. When designing a prioritization process under the amended TSCA, EPA must ensure that the toxicity endpoints are inclusive of important biological systems at all stages of development.

The toxicity endpoints evaluated in any prioritization methodology developed by the Agency must take a systems approach and be widely inclusive of systems important for the proper biological functioning of a wide range of environments and humans at all stages of development. All human systems (e.g., the endocrine, reproductive, and immune systems) are essential for human growth and well-being. The evaluation of endpoints relative to these systems is, therefore, important to include in any prioritization process.

In identifying areas in need of critical evaluation, NRDC recommends that the Agency consult the procedure utilized by the California Department of Toxic Substance Control (DTSC) Safer Consumer Products to identify Candidate Chemicals for evaluation. The DTSC Safer Consumer Products Candidate chemical list was developed using a variety of authoritative lists and evaluated hazard based upon 25 hazard traits, including – reproductive toxicity, respiratory toxicity, carcinogenicity, bioaccumulation, hepatotoxicity, digestive system toxicity, endocrine toxicity, genotoxicity, environmental toxicity, developmental toxicity, neurotoxicity, dermatotoxicity, musculoskeletal toxicity, hematotoxicity, cardiovascular toxicity, ocular toxicity, other hazard trait, nephrotoxicity, urinary system toxicity, digestive system toxicity, genotoxicity, environmental persistence, digestive system toxicity, neurotoxicity, and digestive system toxicity. Hazard trait evaluation based upon authoritative lists allows for the rapid and efficient selection of chemicals with known toxicity.

4. **Exposure categories should be broadened to be more inclusive of the ways in which people are exposed to TSCA-regulated chemicals.**

While the amended TSCA explicitly states that the "exposure potential of a chemical substance or a category of chemical substances (including consideration of persistence and bioaccumulation, potentially exposed or susceptible subpopulations and storage near significant sources of drinking water), the conditions of use or significant changes in the conditions of use of the chemical substance, and the volume or significant changes in the volume of the chemical substance manufacture or processed" shall be considered during the prioritization process, this should not be considered a definitive or finite list. When evaluating exposure potential of a chemical substance or category of chemical substances, the Agency must ensure that a wide range of exposure pathways are considered in the prioritization process. Workplace exposures (and take home exposures – e.g., chemicals on clothing), air emissions, children's products, consumer products, and other relevant categories of exposure must be considered. The agency should also consider cumulative and aggregate exposures when assigning exposure values to chemical substances and categories of chemical substances.

Data gaps and data sources

5. **Chemical substances or categories of chemical substances with data gaps in any of the hazard or exposure criteria must never be classified as "low priority".**

Classification of chemical substances or categories of chemical substances deemed "low" toxicity or "low" exposure should be based on a preponderance of data – which EPA can now more easily obtain using Sections 4, 8 and 11 of TSCA. The default assumption for missing data should be the most protective of public health and the environment – i.e., the highest possible score of harm in the missing data category (level 3 in EPA, 2012 and EPA, 2014). This reading is supported by the statutory emphasis on treating uncertainty as a basis for designating a chemical as "high priority" as embodied in text which dictates that if after a testing order evidence is "insufficient to enable the designation of the chemical

substance as a low-priority substance, the Administrator shall designate the chemical substance as a high-priority substance."[2]

6. Emerging methods in risk assessment cannot be used to classify chemical substances or categories of chemical substances as "low priority" but can be used to identify "high priority" substances.

Emerging methods in hazard, exposure, and risk assessment hold great promise for increasing the speed and breadth of chemical evaluations. New tools such as ToxCast, Tox21, and ExpoCast are rapidly evolving into methods by which to screen large numbers of chemicals across multiple toxicity pathways and exposure scenarios (Wambaugh, 2014; Sipes, 2013; Knudsen, 2011). As outlined in EPA's Next Generation Risk Assessment: Incorporation of Recent Advances in Molecular, Computational, and Systems Biology (EPA, 2014), high-throughput and high-content assays could be useful for prioritizing large number of chemicals for "focused research, further testing, or further assessment".

While the potential exists for emerging tools to be used to identify chemicals with both high and low toxicity and exposure potential, there are several severe limitations that argue against their use for identifying chemicals with low toxicity or exposure potential at this time. The lack of biological coverage, metabolic capacity, replicability, and concordance with animal systems severely limits the capacity of high-throughput systems to accurately identify all chemicals with toxicity – resulting in potentially toxic chemicals being missed in screening (Pham, 2016; Silva, 2015). The inaccuracy of underlying databases, the lack of inclusion of vulnerable populations (including children under the age of six and worker populations), and missing sensitivity analyses for existing models, increases the likelihood that high-throughput exposure models would incorrectly identify and/or predict individual and population-level exposure levels for chemical substances and categories of chemicals substances (Wambaugh, 2014). Additionally, the current systems of rapid exposure and toxicity assessment are extraordinarily limited in their capacity to evaluate risks in ecosystems. The Agency is required to protect both humans and ecosystems, so relying upon tools that focus almost exclusively on human health endpoints would not fulfill EPA's obligations under the law. At this time, the significant limitations of emerging methods in risk assessment make them inappropriate tools for designating "low priority" substances.

Opportunities do exist, however, to use emerging methods to identify chemical substances and categories of chemical substances that could be designated as "high priority". Positive signals within high-throughput or high-content assays could indicate actual toxicity of a chemical substance or category of chemical substances. Public health and environment protective prioritization processes should allow for high false positive rates, to ensure that no toxic chemicals are prematurely and incorrectly identified as lacking risk. The statutory text leans towards designating a chemical as high risk when evidence is unclear.

7. The prioritization process should utilize the chemical categories used in the new chemicals program.

[2] 15 U.S.C. § 2605(b)(1)(C)(iii).

The TSCA New Chemicals Program (NCP) has developed chemical categories informed by significant data on toxicity, hazards, and physico-chemical properties of chemicals (EPA, 2010). For new chemicals that fall within one of these categories, EPA uses data from an appropriate structural analogue to inform the evaluation of hazard and risk: "If a new chemical substance is structurally similar to a substance for which EPA has positive toxicity data and there is sufficient exposure, EPA may regulate that substance…based on its potential unreasonable risk."

By the same token, these NCP chemical categories should be used to group and prioritize existing chemicals. If existing chemicals fall within one of these chemical categories, they should all be considered together and data from the appropriate structural analogue should be used to feed into the prioritization process.

8. **We encourage the use of methods like read-across and grouping chemicals to fill data gaps and assign "high" priority designations, but these must not be limited to narrow or restrictive criteria such as mechanism or mode of action. These methods, in particular molecular weight cut-offs and polymer exemption criteria/ polymers of low concern, should not be used to assign "low" priority designations.**

Chemical groupings to assign high priority should be based on flexible criteria that allow for categorization based upon a host of characteristics including physical and chemical properties, biological similarity, common adverse effect, and functional class (e.g., flame retardants). Basing groupings solely on narrowly defined mechanisms or modes of action would overly restrict chemicals that could be grouped together, particularly for chemicals (e.g. carcinogens) that can act via multiple and varied modes of action (NRC, 2009).

Molecular weight cutoffs should not be used to assign low bioavailability, low hazard, nor low priority. EPA has, in past prioritization and chemical evaluations, inappropriately relied on the non-evidence based assumption that higher molecular weight chemicals (MW>1,000) have limited bioavailability and thus do not contribute to toxicity. But empirical evidence indicates that this "molecular weight cut off" criterion is seriously flawed. For example, polymeric flame retardants with MW>1,000 have been found to contaminate biological specimens such as gull's eggs. These findings reveal that substances with higher molecular weights can exhibit bioavailability, and that a molecular weight cut-off criterion cannot be used to determine bioavailability with enough reliability. Bioavailability should be determined based on empirical evidence and other well-established physico-chemical properties.

Furthermore, a low bioavailability prediction in of itself is not sufficient to establish low hazard. Unless there are specific data to the contrary, it is inappropriate to assume that low expected bioavailability results in low hazard. The flame retardant DecaBDE was long thought to be "inert" and low hazard because of low bioavailability. We now know that this prediction was quite wrong, as metabolic transformation creates highly toxic products (Betts, 2004).

The same reasoning on bioavailability and hazard was used to create polymer exemption criteria/ polymers of low concern criteria. Therefore, these criteria should not be used either to assign "low priority" designations for polymers.

9. **EPA should include chemicals for which it is already taking some form of regulatory action in the pool of chemicals evaluated for prioritization.**

Chemicals for which the Agency is already taking action should not be excluded from prioritization decisions under the amended TSCA. In the prior Work Plan Prioritization methodology (EPA, 2012) several chemicals that "may pose unreasonable risk" (including polymers, metals principally identified as toxic to the environmental, and chemicals subject to Action Plans or significant regulation under TSCA), were excluded from its Work Plan list due to other activities or regulatory actions being taken. The practice of excluding chemicals like mercury from the 2012 Work Plan Prioritization methodology, and thereby in effect assigning them a "low priority" status, should be eliminated from the prioritization process.

Methodological Requirements for Prioritization Under the Amended TSCA.

In its 2012 *TSCA Work Plan for Chemical Assessments: Methods Document* (EPA, 2012), the Agency outlined a two-step process in which to screen and prioritize chemicals for further assessment. NRDC views the Work Plan Methodology as a good first step, and has several suggestions for ways in which to enhance, improve, and expand upon the existing framework. We support the use of authoritative lists as reliable and scientifically sound sources of information and appreciate the Agency's need to create a transparent and robust system for prioritization. As a screening level process, we fully support a wide-reaching tool that allows the agency the flexibility to accurately and efficiently identify chemical substances or categories of chemical substances that "may pose an unreasonable risk" to humans or the environment.

1. **When evaluating chemicals for further evaluation under the two-step Work Plan prioritization process, the Agency should use a wide range of criteria and data sources in order to consider the risks of as many chemical substances and categories of chemical substances that may pose harm as possible.**

NRDC supports the use of broad criteria based upon authoritative lists and other sources of information to serve as a primary screen for chemicals requiring additional prioritization-based evaluation. The current factors (i.e., potential concern for children's health, neurotoxic effects, probable or known carcinogens, use in children's products, detection in biomonitoring programs, and persistence and bioaccumulations) are useful starting points, but should be expanded to cover additional exposure and toxicity endpoints. The Agency should expand the toxicity endpoints to include other relevant biological systems for humans and ecosystems (e.g., immune, endocrine, cardiovascular, and respiratory systems), and should explore the use of hazard traits for identifying chemical hazard (see bullet 3 in Endpoint Evaluation section, above). EPA should also extend carcinogenic effects to include possible human carcinogens (IARC classification 2B) given the "may pose unreasonable risk" criteria set forth in the amended TSCA.

In identifying sources of information, the current list established by the Agency should be expanded to include information generated by states, sister federal agencies, and international governments. For

example, databases generated by the State of California (Prop. 65[3], chemicals in the California Environmental Contaminant Biomonitoring Program[4], Safer Consumer Products Candidate Chemical List[5]), other federal agencies (e.g., ATSDR Neurotoxicants List[6], NTP Report on Carcinogens, and NTP OHAT reproductive and developmental toxicants list), and other international governments (e.g., European Union candidate chemical list of Substances of Very High Concern[7], EC PBT list, EC Annex VI respiratory sensitizers, EC endocrine disruptors, EC Annex VI CMRs, and the European Chemicals Agency (classification and labeling database[8]) should be considered viable and reliable sources of information for identifying chemical hazards. The US EPA Integrated Risk Information System (IRIS) is an authoritative and reliable program that must also be included. We recommend including all the hazard trait lists identified and used by the CA Safer Consumer Products program.[9]

When creating factors for preliminary exposure screening, the Agency should also expand the current criteria beyond children's products to include other more general exposure routes. For example, exposure to chemicals via consumer products in general, furniture, air, water, and other routes should be included in the step one prioritization criteria. EPA should also expand the data sources used to identify human exposures including California Prop. 65, National Human Adipose Tissue Survey (NHATS), National Human Exposure Assessment Survey (NHEXAS), Total Exposure Assessment Methodology (TEAM), the NIH Hazardous Substances Data Bank[10], and the Danish Consumer Product Studies. We recommend including all the exposure potential lists identified and used by the CA Safer Consumer Products program.[11] Though NHATS, NHEXAS, and TEAM are older datasets, discounting the information in these studies without demonstrated decreases in chemicals identified in the studies would limit potentially rich sources of information.

Caution should be exercised, however, when using biomonitoring data as a source of exposure criteria. The vast majority of chemicals currently reside outside of measurement via modern analytical techniques, rendering them impossible to detect in biomonitoring studies. Biomonitoring information should therefore be used to positively identify a chemical as having known exposure, but should not be used to exclude chemicals from further classification.

2. For chemicals with missing data in any of the preliminary prioritization (step 1) criteria, the default assumption should be that the chemical automatically requires additional evaluation.

[3] http://oehha.ca.gov/proposition-65/proposition-65-list
[4] http://www.biomonitoring.ca.gov/
[5] https://calsafer.dtsc.ca.gov/chemical/search.aspx
[6] http://www.atsdr.cdc.gov/substances/toxorganlisting.asp?sysid=18
[7] https://echa.europa.eu/candidate-list-table
[8] https://echa.europa.eu/information-on-chemicals/cl-inventory-database?p_p_id=dissclinventory_WAR_dissclinventoryportlet&p_p_lifecycle=0&p_p_state=normal&p_p_mode=view&p_p_col_id=column-1&p_p_col_pos=1&p_p_col_count=2
[9] https://www.dtsc.ca.gov/SCP/SourceLists.cfm
[10] https://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB[11] https://www.dtsc.ca.gov/SCP/SourceLists.cfm
[11] https://www.dtsc.ca.gov/SCP/SourceLists.cfm

Missing information in the first step of the prioritization process should not be a *de facto* way for chemicals to evade further prioritization and evaluation. Chemicals that have missing information for any of the factors identified during step 1 should be placed in a separate pool for data requests (as authorized under Sections 4, 8 and 11 of the amended TSCA) and further evaluation. If new information about a chemical substance is not obtained in a timely manner, and if EPA proceeds with proposing a priority designation, chemicals would generally then be placed into the step 2 pool (see Figure 1). Under no circumstances should a chemical with data gaps be designated as "low priority".

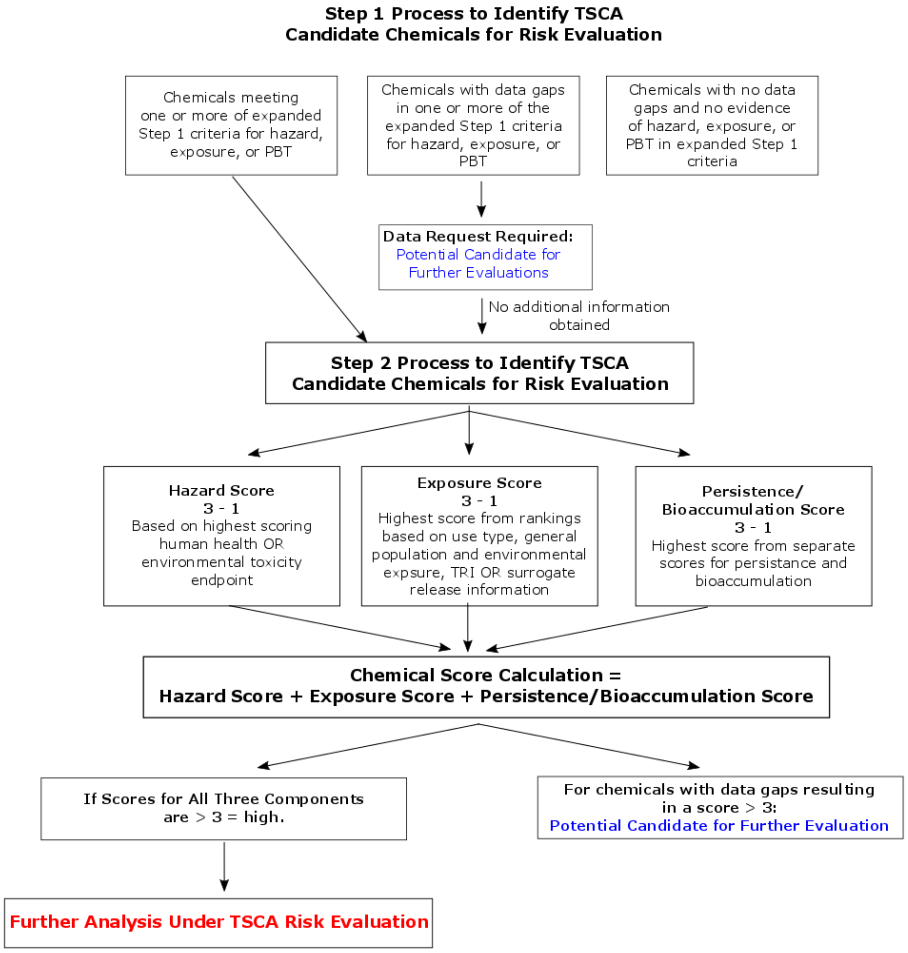

Figure 1. Key elements of a prioritization work plan (modified from the Work Plan Prioritization Methodology; EPA, 2012).

3. The Chemical Score Calculation in step 2 of the Work Plan Methodology must be amended to use the highest score rather than normalized scores for exposure and persistence, bioaccumulation, and toxicity (PBT) characteristics.

In the evaluation of exposure and PBT characteristics in step 2, the highest scoring rather than normalized score should be used – similar to the hazard score (see Figure 1). Normalized scores in exposure and persistence/bioaccumulation allow low scores in each category to effectively "pull down" high scores in these categories. This effectively creates a scoring mechanism in which required

components of the overall score of a chemical are weighted toward diminished risk. By using the highest score across all three evaluation factors (i.e., hazard, exposure potential, and persistence/bioaccumulation), the Agency will create a more inclusive list of chemicals that "may pose an unreasonable risk" to populations and ecosystems, particularly vulnerable populations.

4. **If EPA proposes a priority designation in the absence of data for any hazard, exposure, or persistence/bioaccumulation, the chemical should, by default, receive the highest score in that category.**

For chemicals with data gaps in exposure, hazard, or PBT characteristics, the default assumption should be that the chemical has the highest score in that particular category. This creates an incentive for data generation and dissemination, and prevents possibly harmful chemicals from evading evaluation due to a lack of information. Chemicals with data gaps can be classified as a "Potential Candidate for Information Gathering" chemical or could be placed into the pool of chemicals requiring further analysis and expanded risk evaluation (see Figure 1).

5. **When combining scores and ranking chemicals based upon the Chemical Score Calculation, the thresholds for "low", "medium", and "high" scores (as defined in the 2012 Work Plan Prioritization Methodology; EPA, 2012) should be shifted to be more inclusive of uncertainty and vulnerable and susceptible populations.**

In determining "low" and "high" priorities under the ranking system, the scoring system should be shifted to be more inclusive of chemicals with potential risk in humans and ecosystems to take into account uncertainties in underlying data sources (e.g., production volume data) and variability in susceptibility (e.g., critical windows of development) and exposure (e.g., highly exposed populations like workers or disproportionately exposed communities). Chemical substances or categories of chemical substances with chemical score calculations greater than 3 using the revised methodologies proposed in these comments (e.g., highest score prevails, chemicals with data gaps excluded, authoritative sources of information; see Figure 1) should be considered candidates for "high priority" classification. In other words, a "medium" score under the Work Plan Prioritization Methodology should translate to a "high" score classification under the modified prioritization procedure (see Figure 1).

Conclusion

NRDC appreciates the opportunity to provide comments on the Risk-Based Procedural Rule for Chemical Prioritization under the amended TSCA. We look forward to working with the Agency in the implementation phase of the amended law and would be pleased to discuss the comments and recommendations articulated in these comments at your convenience. To schedule a phone call or meeting, please contact Daniel Rosenberg, Senior Attorney – Health and Environment Program, Natural Resources Defense Council at drosenberg@nrdc.org or (202) 289-6868.

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