March 20, 2017

Comments from the Natural Resources Defense Council on Proposed Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act

Submitted to Docket EPA-HQ-OPPT-2016-0654

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 2.8 million members and online activists. NRDC does not have any financial interest in the topic of these comments.

NRDC welcomes the opportunity to comment on EPA's proposed "Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act" (Risk Evaluation Rule) (82 Fed. Reg. 7562) (January 19, 2017). The proposed rule, along with several other rules EPA currently has underway, will establish the ground rules for implementation of the revised Toxic Substances Control Act ("TSCA"), setting the stage for what many hope will be a new era in which EPA comprehensively evaluates chemicals of concern and imposes effective restrictions on those that pose an unreasonable risk of injury to health and the environment.

The Agency has proposed a strong and sound rule that is consonant with the requirements of the law and requires only clarification in some places to ensure consistency between the statute, preamble and the actual rule. No significant revisions to the proposed risk evaluation rule are needed. Failing to meet the statutory deadlines for finalizing rules on risk evaluation and risk prioritization will have a domino effect that will quickly derail implementation of central elements of the new law before it has really gotten underway. For example, to meet the law's deadline for initiating risk evaluations for the first 20 "high priority" chemicals no later than 3.5 years from the date of enactment, EPA must begin the process fairly soon of information-gathering as envisioned in the Agency's proposed Prioritization Rule to inform both the prioritization and scoping steps of implementation. While 3.5 years may seem like a long time from now, in fact that time will be quickly filled with precedent steps including information gathering, data analysis, and several rounds of public comment. EPA must remain on schedule or the framework for actions under TSCA will be damaged and the quality of EPA decision-making could suffer. We urge EPA to finish the job it began in June 2016 and complete the final rulemakings for risk evaluation, prioritization and scoping within the one year deadline established by Congress.

Background

TSCA is the most important federal law for assessing and regulating the use of industrial chemicals, including those used in commercial and consumer products. The public is regularly exposed to hundreds if not thousands of chemicals, some of them on a daily basis, from before we are born and throughout our lives. Many chemicals to which the public is routinely exposed are known to be unsafe, associated with a variety of serious health effects including learning and developmental delays, infertility, birth defects and cancer. For many more chemicals, insufficient information is currently available to EPA or

the public to determine whether they are hazardous to human health or the environment.

All Americans benefit from living in a safe environment, including air, drinking water, land, and an indoor environment free from toxic chemicals. The personal benefits for individuals, families, friends and communities of not having to contend with illness and disease are obvious. In addition, the benefits of reducing exposure to toxic chemicals will accrue to the nation as a whole, in the form of reduced health care costs, greater work productivity, improved academic achievement and healthy and thriving communities. Improvements in all these areas are within our grasp if we seize the opportunity to gain control over the chemicals that routinely pollute both the outdoor and indoor environment.

The recent revisions to TSCA provide the Agency with the opportunity to overcome a legacy of underachievement – a legacy largely due to problems with the original law -- and finally begin to tackle the immense task of obtaining information about chemicals of concern, evaluating the potential effects of the chemicals, and taking regulatory action to protect the public from those chemicals that pose a risk to public health. To be successful in this task, EPA must meet the deadlines set under the revised statute and follow the law's requirements to comprehensively assess the conditions of use of chemicals and to protect the public including vulnerable populations.

Summary

Our detailed comments below are divided into the following three sections:

1. Legal Requirements
2. Suggestions for EPA's Proposal
3. Strengths of EPA's Proposal.

1. Legal Requirements

1(a) The Administrative law context for the risk evaluation rule.

EPA is under a statutory obligation to issue final prioritization and risk evaluation rules by June 22, 2017.[1] This Congressional directive to finalize the rules quickly is evidence of frustration after decades of Agency inaction on TSCA and the need for EPA to swiftly implement the newly strengthened TSCA risk evaluation process. The lack of mandatory deadlines was discussed repeatedly in testimony and other commentary about the original version of the legislation that ultimately resulted in the new law enacted in June 2016.[2, 3] The need for mandatory, enforceable deadlines was accepted fairly quickly by all stakeholders as an essential element of TSCA legislation and it became a key element of future drafts and versions of legislation in both the House and Senate.

Significantly, in November 2016, a bi-partisan group of Senators, led by Senators James Inhofe of Oklahoma and Tom Udall of New Mexico, wrote a letter to Vice President-Elect Pence urging prompt and effective implementation of TSCA by the new Administration, including stressing the importance of the new EPA Administrator "appreciating" the deadlines in the revised law.[4] The letter noted the new law "requires [EPA] to make many critical decisions in the first months and years of the program" and

[1] See https://www.epa.gov/sites/production/files/2016-06/documents/june_30_webinar_ppt.pdf. The Frank R. Lautenberg Chemical Safety for the 21st Century Act. June 2016. United States Environmental Protection Agency (EPA).

[2] See for example separate testimony from Ansje Miller, Eastern States Director, Center for Environmental Health; Nancy Buermeyer, Senior Policy Strategist, Breast Cancer Fund; Daniel Rosenberg, Senior Attorney, NRDC from Senate Environment and Public Works Committee Hearing: "Strengthening Public Health Protections by Addressing Toxic Chemical Threats" (July 31, 2013); and blog from Safer Chemicals Healthy Families, "SCHF Issues Position on Chemical Safety Improvement Act" (June 11, 2013); and Safer Chemicals Healthy Families full-page ad in Congress Daily, "Make it Stronger" (July 31, 2013) (https://twitter.com/hashtag/MakeItStonger?src=hash&ref_src=twsrc%5Etfw)

[3] See for example, "Testimony of Jim Jones, Assistant Administrator, Office of Chemical Safety and Pollution Prevention, U.S. Environmental Protection Agency, Before the Energy and Commerce Committee, Energy and Environment Subcommittee, United States Congress" (April 14, 2015)

[4] See attachment 1.

noted that the Agency "has a crucial role to play in ensuring that the promise of the new law is realized." The Senators stated their expectation that EPA would "vigorously implement the new law" including "moving expeditiously to identify and address chemicals with the greatest potential impact on public health, especially affecting vulnerable populations expressly required to be protected in the Act, including pregnant women, children, workers, and other at-risk communities." The letter concluded that "it is essential to maintain momentum during the Presidential transition and in the early months of the new Administration to ensure that this new law is successful."

There is no question that after 40-years of almost total inaction to address the threats posed by the thousands of grandfathered "existing" chemicals, Congress intended EPA to move forward steadily and on schedule to fulfill its obligations under the new law. It is troubling then that in a recent public meeting held by EPA to take public comment on the scoping process and the first 10 chemicals EPA has selected for risk evaluation, representatives of the chemical manufacturer's trade association suggested that EPA should not worry about the statutory deadlines and instead focus on "getting it right." EPA should ignore this poor advice and fulfill its mandatory duties under the law, including meeting its deadlines for completing rulemakings on risk evaluation, prioritization, and scoping. In the preamble to the proposed rule, EPA appropriately emphasizes meeting its statutory responsibilities, and there is no reason for the Agency to deviate from that course in the final rule.

For the same reasons, due to the statutory deadlines in TSCA, the prioritization and risk evaluation rules are not subject to Executive Order 13771, since the express language of the Order indicates it does not apply "where prohibited by law." EPA cannot comply with the Order *and* meet its TSCA obligations for finalization by June.[5] Nor do these rules come close to triggering the $100 million cost thresholds for applying the Executive Order, as specified in the accompanying guidance.[6]

When issuing the final rules, EPA also must bear in mind its obligations to provide adequate public notice and comment under the Administrative Procedures Act ("APA"). EPA cannot reverse course from the proposed rules without limitation. The contents of the final rules must be a 'logical outgrowth' of the rule it originally proposed."[7]

As part of the rulemaking process, agencies are required to "describe the range of alternatives being considered with reasonable specificity. Otherwise, interested parties will not know what to comment on, and notice will not lead to better-informed decision making."[8] A provision in the final rule that has "no roots in the agency's proposal" cannot be a logical outgrowth because "[s]omething is not a logical outgrowth of nothing."[9]

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[5] NRDC has also challenged the constitutionality of the Executive Order, since it directs federal agencies to violate the laws that govern rulemaking – laws that neither require nor allow the kind of cost-only analysis and cost-based trading the Executive Order mandates.

[6] See https://www.whitehouse.gov/the-press-office/2017/02/02/interim-guidance-implementing-section-2-executive-order-january-30-2017. EPA estimated annual costs of $69,353 for the risk evaluation rule (82 FR 7574), and did not estimate any costs to the regulated community for the prioritization rule.

[7] Northeast Maryland Waste Disposal Auth. v. E.P.A., 358 F.3d 936, 951 52 (D.C. Cir. 2004) (per curiam)

[8] Small Refiner Lead Phase-Down Task Force v. U.S. E.P.A., 705 F.2d 506, 549 (D.C. Cir. 1983).

[9] Envtl. Integrity Project v. E.P.A., 425 F.3d 992, 996 (D.C. Cir. 2005) (quoting Kooritzky v. Reich, 17 F.3d 1509, 1513 (D.C. Cir. 1994)).

For example, an unexpressed intention cannot convert a final rule into a logical outgrowth.[10]. The rationale behind requiring agencies to follow the notice-and-comment rulemaking procedure is to alert the public of new rules and regulations and to provide those interested parties with the opportunity to participate in the rulemaking process.[11] In order for the notice-and-comment process to function as designed, "[i]nterested parties cannot be expected to divine [the agency's] unspoken thoughts."[12]

Agencies cannot rely solely on comments to show they complied with the APA's notice requirements. "As a general rule, [an agency] must itself provide notice of a regulatory proposal. Having failed to do so, it cannot bootstrap notice from a comment."[13] Thus, EPA is limited in the degree to which it may diverge from what it has proposed without triggering the need for a re-proposal of its rule. And in any case, no such re-proposal is needed as the proposal is sound and consistent with the statute, requiring only clarification in a few places as discussed herein.

1(b) The law requires the Agency to evaluate risks associated with all known, intended, and reasonably foreseeable activities related to a chemical substance.

In its proposed risk evaluation rule, EPA interprets the revised TSCA as requiring the Agency to consider all uses encompassed within conditions of use during risk evaluation, and accordingly structured the risk prioritization and scoping processes to obtain and assess information based on this "comprehensive" approach to chemical management.[14] Similarly, in its proposed prioritization rule, EPA reiterated its interpretation that the amended TSCA requires EPA to evaluate all uses of a chemical that constitute the conditions of use, as the best way to meet its statutory obligations and the purpose underlying the revisions of the law.[15] EPA has already formalized this interpretation in denying a citizen petition under TSCA.[16]

NRDC agrees with EPA's interpretation, and indeed believes this reading of the law is compelled by statutory construction and legislative history.[17] Specifically, the statute directs EPA to determine whether a chemical presents an unreasonable risk of injury to health or the environment under "the conditions of use" and to establish a risk evaluation process to conduct this inquiry.[18] In provision after provision, EPA is directed to evaluate the chemical under "the conditions of use." [19]

"Conditions of use" is expressly defined to mean "the circumstances, as determined by the

[10] Shell Oil Co. v. E.P.A., 950 F.2d 741, 751 (D.C. Cir. 1991)
[11] Int'l Union, United Mine Workers of Am. v. Mine Safety and Health Admin., 407 F.3d 1250, 1259 (D.C. Cir. 2005)
[12] Shell Oil Co., 950 F.2d at 751.
[13] Small Refiner, 705 F.2d at 549
[14] *See* Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act, 82 Fed. Reg. 7562, 7565-6 (January 19, 2017).
[15] *See* Procedures for Prioritization of Chemicals for Risk Evaluation Under the Toxic Substances Control, 82 Fed. Reg. 4825, 4829 (January 17, 2017).
[16] Fluoride Chemicals in Drinking Water; TSCA Section 21 Petition; Reasons for Agency Response, 82 Fed. Reg. 11878, 11880 (February 27, 2017).
[17] Therefore, we do not believe different readings of the law are possible, as suggested by the Agency at 82 Fed. Reg. 7565.
[18] 15 U.S.C. § 2605(b)(4)(A), (B).
[19] *See, e.g.,* 15 U.S.C. § 2605(b)(1)(B), (b)(4)(F).

Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of."[20] Under this statutory definition, and in the various applications of the term in the law, including but not limited to the risk evaluation determination, there are no exceptions embedded in either the definition or in the application of the term when it is used. This absence of discretion to ignore uses for risk evaluation purposes is consistent with the legislative history supporting the comprehensive evaluation of a chemical.[21]

Furthermore, as EPA notes, EPA is required to evaluate the "chemical substance,"[22] not particular uses of the chemical in question. If the statute were interpreted to allow EPA to evaluate only a subset of uses of a chemical substance, the chemical substance could be determined to not pose an unreasonable risk based on the consideration of minor uses of the chemical, even when other more significant uses were known or foreseen. This would not facilitate a consideration of the chemical substance as a whole, and thereby would undermine the statutory scheme.

In addition, an interpretation providing the Agency discretion to ignore conditions of use would violate the statutory construction as applied to the designation of low priority substances under Section 6(b)(1)(B)(ii) of TSCA. By definition, low priority substances are chemicals found by EPA not to present an unreasonable risk to health and the environment, including to a potentially exposed or susceptible subpopulation, "because of *a* potential hazard and a potential route of exposure under the conditions of use." (Emphasis added). A single hazard or exposure "under the conditions of use," broadly defined in the statute, is sufficient to compel a high-priority designation.[23] Where EPA lacks sufficient information regarding a substance, the default designation is "high priority," under Section 6(b)(1)(C)(iii) of TSCA. This default mechanism demonstrates the statutory obligation to perform a comprehensive chemical evaluation. EPA discretion to ignore some conditions of use would undermine the very purpose of the default mechanism – to confine low priority designations to chemicals which do not present an unreasonable risk under *any* conditions of use.[24]

This plain language reading is reinforced by the statutory directive to evaluate aggregate exposures, where relevant, because aggregate exposure assessments cannot be effectively conducted if all uses contributing to aggregate exposures are not considered. Evaluating the total exposure to a chemical is essential for assessing unreasonable risk to potentially exposed or susceptible populations, as directed by the statute.[25]

As EPA notes, Section 6(b)(4)(F)(i) of TSCA requires that, in conducting a risk assessment, the Administrator "*shall* . . . integrate and assess available information on hazards and exposures . . .

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[20] 15 U.S.C. § 2602(4).

[21] *See* Senate Floor Debate, 162 Cong. Rec. S3511-01, S3516 (Jun. 7, 2016) (Analysis and Views of Democratic Members (Boxer, Markey, Udall, Merkley), in regards to the "conditions of use" definition: "In fact, a new definition added to TSCA explicitly provides such authority [to consider reasonably anticipated uses in evaluating risk] and a *mandate* for EPA to consider conditions of use that are not currently known or intended but can be anticipated to occur.") (Emphasis added). If EPA had the discretion to ignore certain uses, there could be no mandate to consider future uses because the discretionary exception would swallow the rule.

[22] 15 U.S.C. § 2605(b)(4)(A).

[23] *See* 82 Fed. Reg. 4830.

[24] *See* 82 Fed. Reg. 4827. NRDC supports proposed 702.11(d) as a codification of this statutory text and intent.

[25] 15 U.S.C. § 2605(b)(4)(A).

including information that is relevant to specific risks of injury to health and information on potentially exposed or susceptible subpopulations." (Emphasis added). A "potentially exposed or susceptible subpopulation" is defined as "a group of individuals within the general population . . . who, *due to either greater susceptibility or greater exposure*, may be at greater risk" of adverse effects.[26] As the definition makes clear, risks to potentially exposed or susceptible subpopulations are premised on greater exposure or susceptibility. For such a subpopulation, a failure to consider the sum of all known or reasonably foreseeable additive exposures would constitute a failure to meet both the Section 6(b)(4)(F)(i) obligation to assess information relevant to susceptible populations, and the fundamental Section 6 obligation to protect potentially exposed or susceptible populations from unreasonable risk.

For example, when evaluating lead, EPA must identify the populations at risk (i.e., young children) receiving the "greater exposures," which requires consideration of aggregate exposures from the various relevant sources, including drinking water, emissions from industrial sources, consumer products, and lead paint in the home, since the risk to children from lead arises from their total exposure. The lead risk evaluation results would be based upon the impacts of the aggregate exposures to the children with the "greater exposures."

Indeed, in assessing exposures, the statute imposes an explicit "requirement" that EPA "take into account, where relevant, the likely duration, intensity, *frequency, and number of exposures* under the conditions of use of the chemical substance,"[27] and repeatedly refers to the EPA's consideration of whether a "combination of activities" involving the chemical presents a risk to health or the environment.[28] To consider the aggregate exposure from the frequency and number of exposures considered or the "combination of activities," EPA must look across the full spectrum of a chemical's use and disposal.

In sum, in light of the plain language of the statute requiring consideration of "the conditions of use," without exception; the requirement to evaluate chemical substances, not particular uses; and of the

[26] 15 U.S.C. § 2602(12) (emphasis added).

[27] 15 U.S.C. § 2605(b)(4)(F)(iv) (emphasis added). NRDC agrees with EPA's proposal to include this language in the regulations concerning "exposure assessment," 82 Fed. Reg. 7579; this appropriately incorporates the statutory requirement to consider aggregate exposures where relevant. Similarly, NRDC agrees with EPA's proposal to include the statutory requirement to "describe whether aggregate or sentinel exposures . . . were considered, and the basis for the consideration," 15 U.S.C. § 2605(b)(4)(F)(ii), in the regulatory sections concerning "risk characterization and peer review procedures." *See* 82 Fed. Reg. 7579. Unlike the substantive requirement to consider the frequency and number of exposures, this procedural provision simply imposes a descriptive requirement: to "describe" the nature and basis of the analysis. It does not modify the requirements of the exposure assessment to consider the "duration, intensity, frequency, and number of exposures" and thus the obligation to perform aggregate exposures, where relevant.

[28] *See, e.g.,* 15 U.S.C. § 2605(a) (stating that "If the Administrator determines in accordance with subsection (b)(4)(A) that the manufacture, processing, distribution in commerce, use, or disposal of a chemical substance or mixture, or that *any combination of such activities*, presents an unreasonable risk of injury to health or the environment . . .") (emphasis added); § 2605(d)(3)(A) (referring to the Administrator's consideration of the effects of "the manufacture, processing, distribution in commerce, use, or disposal of the chemical substance or mixture subject to such proposed rule or *any combination of such activities*") (emphasis added); § 2604(b)(2)(B) (requiring manufacturers or processors of new chemicals or of significant new uses of a chemical to submit information showing that "the manufacture, processing, distribution in commerce, use, and disposal of the chemical substance or *any combination of such activities* will not present an unreasonable risk of injury to health or the environment") (emphasis added).

requirement to evaluate aggregate exposures, where relevant, TSCA as revised compels EPA to evaluate all known, intended, and reasonably foreseeable activities associated with a chemical, as embodied in "the conditions of use."[29]

1(b)(i) Intended, known or reasonably foreseeable are independent descriptors of conditions of use.

We now turn to what are considered "intended, known, or reasonably foreseeable" circumstances under the law. These are three separate and independent descriptors of the circumstances constituting conditions of use, and therefore EPA must give meaning to *each* of the descriptors when identifying conditions of use for a particular chemical.

Some have suggested these descriptors preclude EPA's consideration of conditions of use which violate federal environmental or workplace regulations, exposures inconsistent with labels, and/or uses inconsistent with the manufacturer's intended use of a chemical or product.[30] However, as explained below, such limitations would violate the statute since they fail to give independent meaning to each of the descriptors. Moreover, EPA's mandate to protect "potentially exposed or susceptible populations," as the term is defined in the law, precludes EPA from summarily dismissing such conditions of use without considering whether existing regulations adequately protect such populations.

For example, the manufacturer's intended use of a chemical or product is only one descriptor applying to the conditions of use. Where the manufacturer knows the chemical or product is actually used in other ways, the public knows of other uses, and/or the Administrator can reasonably foresee other uses (for example based upon the chemical or product's properties and functionality), the statute compels EPA to identify such conditions of use. The reality is chemicals and products are often used in multiple ways, particularly if there are no legal constraints against such uses, and these conditions of use cannot be rejected simply because the manufacturer alleges it never intended those uses (while profiting from the sales).[31]

The same legal analysis holds true for chemical or product labels, which may largely reflect manufacturer intent. Moreover, in the case of labels for consumer products particularly, adherence to label use instructions cannot be assumed as a factual matter, particularly where the public and EPA "knows," or EPA can reasonably foresee, exposure scenarios inconsistent with labels. Indeed, EPA recently identified 48 relevant studies or meta-analyses concluding consumers and professionals do not follow the advice on the label for a variety of reasons.[32]

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[29] We are compelled to address EPA's statement in the preamble that an activity constitutes a condition of use . . . "only if EPA determines that it does" and that "EPA has authority to exercise judgment in making its determination of whether a condition of use is known, intended or reasonably foreseen." 82 Fed. Reg. 7566. While EPA must apply the definition of "conditions of use" to specific circumstances, the Agency lacks discretion to determine that an activity that otherwise meets the definition can be disregarded.

[30] *See*, *e.g*., Comments of the American Chemistry Council to Inform EPA's Rulemaking on the Conduct of Risk Evaluations Under the Lautenberg Chemical Safety Act, August 24, 2016, p. 10.

[31] Indeed, one potential outcome of the Section 6 regulatory process is a risk management rule prohibiting the very uses the manufacturer claims it does not intend.

[32] Trichloroethylene; Regulation of Certain Uses Under TSCA § 6(a), 81 Fed. Reg. 91592, 91601 (December 16, 2016).

Even in the case where federal environmental or workplace standards apply, the relevant considerations are what is known to the Agency or the public, or what EPA can reasonably foresee, regarding uses and exposures related to the chemical. This will be a fact-based, chemical-specific inquiry, which may lead EPA to conclude exposures can exceed the relevant standards, or that the regulations themselves were not set (or adequately complied with) to protect the susceptible populations EPA is charged to protect under Section 6 of TSCA. The reality is some standards are either outdated or intended to protect the general population, not the vulnerable populations specially targeted for protection under the revised TSCA.

The presence of a chemical in a product or waste stream as an impurity or byproduct does not affect the conditions of use definition or scope. Its existence will generally be "known" or "reasonably foreseen" by the manufacturer or EPA. The uses and exposures associated with impurities or byproducts can be significant and their contribution to overall exposure and risk must be accounted for in EPA's risk evaluations.

EPA must also consider uses and potential routes of exposure that are not under EPA's regulatory jurisdiction under TSCA, including in food processing and packaging, and via use in such items as personal care products and cosmetics. The risk evaluations conducted by EPA cannot accurately assess whether a chemical poses an unreasonable risk if all such uses and potential sources of exposure are not accounted for. Whether and how to address uses and potential sources of exposure that are found to contribute to an unreasonable risk is a matter for the risk management stage of the process, including potential exercise of the Agency's authority under Section 9 of TSCA.

1(c) EPA must use information gathering authorities to facilitate risk evaluation.

EPA has appropriately structured the risk prioritization and evaluation processes to obtain the necessary information on a chemical as early as possible in these processes. In the preamble of the risk prioritization rule, EPA indicates it "generally expects" to use the full suite of TSCA information gathering authorities, particularly those under Sections 4, 8 and 11(c) of TSCA, to develop the needed information.[33]

Similarly, in the preamble to the risk evaluation rule, EPA indicates it "generally expects" to exercise as needed its information gathering authorities under Section 8 of TSCA "very early" in the risk evaluation process, and seeks comment on whether and how to incorporate the Section 8 authorities into the risk evaluation rule.[34]

Unfortunately, the text of the proposed rules does not reflect the intent expressed in the preambles. In this section we comment on how EPA's information gathering authorities are best incorporated into both the risk prioritization and risk evaluation rules to facilitate an efficient and effective risk evaluation process under the revised TSCA.

In proposed 40 CFR 702.5(d) of the risk prioritization rule, EPA stresses the importance of developing the information necessary for a risk evaluation as early as possible, preferably before the risk prioritization is formally initiated. NRDC agrees with this approach, yet under proposed 40 CFR 702.5(e) of the risk

[33] 82 Fed. Reg. 4831 (January 17, 2017), col. 2.
[34] 82 Fed. Reg. 7572-3 (January 19, 2017).

evaluation rule, where the Agency lacks sufficient information to proceed with prioritization of a chemical, the proposed text merely provides that EPA "may" use its information gathering authorities to fill the data gaps.

This term, "may" is problematic, particularly as applied to the chemicals on the 2014 update of the TSCA Work Plan for Chemical Assessments. The use of the term "may" is inconsistent with EPA's statutory mandate to ensure that a minimum number of chemicals are undergoing risk evaluation, and EPA's proposed rule must meet this statutory obligation.[35] EPA *must* use its information authorities as needed to meet the statutory mandates for completing the requisite minimum number of risk evaluations, inclusive of the Workplan Chemicals. Lack of information does not constitute a justification for noncompliance where EPA has not utilized the information gathering authorities provided by Congress for this very purpose.

Similarly, under proposed 40 CFR 402.7(f), the text provides that EPA is "likely" to use its information gathering authorities to generate the needed information. While "likely" is better than "may," neither term is consistent with the Agency's aforementioned obligations or the preamble. Consequently, for both regulations (40 CFR 702.5(e) and 40 CFR 402.7(f), we recommend that EPA reflect the preamble intent in the regulatory language by replacing the relevant language with the phrase "EPA shall use its information gathering authorities under the Act as needed to meet the Agency's risk evaluation obligations under the Act."

In addition, NRDC supports revising the proposed risk evaluation rules to reflect the Agency's idea of expressly incorporating the Section 8(d) authorities into the information required from a manufacturer in any request for a risk evaluation under 40 CFR 702.37.[36]

Finally, the Agency's internal procedures must facilitate the systematic use of the Agency's Section 8(d) authorities to compel the submission of unpublished industry conducted health and safety studies as part of the prioritization process. When EPA initiates the prioritization process for a high priority chemical under proposed 40 CFR 702.9, EPA should include as part of (or publish in conjunction with) the Federal Register notice, a proposed Section 8(d) rule (unless such a rule was already issued during the screening process) requiring the submission of unpublished health and safety studies. EPA should finalize this Section 8(d) rule along with the final priority designation, and require submissions within a time frame that facilitates incorporation of the information into the scoping document. By following this approach, EPA will have a more complete hazard and exposure database upon which to base its scoping document and conduct the risk evaluation.

In summary, we agree conceptually with front-loading the collection of information necessary to implement the prioritization and risk evaluation processes, and the consideration of the information available to the Agency. But with this approach comes the responsibility (and the mandate) to fully utilize available authorities to obtain the necessary data in a systematic, comprehensive, and timely manner. EPA should issue final rules and develop internal working processes to reflect this responsibility and mandate.

[35] See 15 USC 2605(b)(2)B), and 15 USC 2605(b)(2)(C), and 40 CFR 702.13(d) as proposed.
[36] See 82 Fed. Reg. 7573 (January 19, 2017), col. 1.

1(d) EPA may not consider alternatives during risk evaluation.

While NRDC shares EPA's concern over the regrettable substitution of toxic chemicals, and support the identification of safer alternatives (including non-chemical alternatives) to chemicals that pose an unreasonable risk, we want to clarify that the consideration of potential alternatives substitute chemicals during the risk evaluation process is premature, contrary to law, and may be counterproductive in some cases.

Once the priority chemical designation is made, this is followed by a 3-3.5 year risk evaluation process, and then a 2-4 year rulemaking to set risk management standards. The effective date of the risk management standards may extend up to five years from the date of promulgation, and EPA is expressly authorized under Sections 6(c) and (d) of TSCA to consider the availability of safer alternatives when setting the effective date of the risk management rules. Accordingly, industry may have about ten years to develop safer substitutes for the chemical in question. EPA should not be making decisions about alternatives before the industry has the opportunity to innovate, given the technical capacity of the industry to change quickly when properly motivated.

Moreover, even in the unlikely event the availability of a safer substitute remains at issue after this time has expired, EPA also retains the authority under Section 6(g) of TSCA to issue an exemption for essential uses where no safer alternative is available. This exemption can be extended until a safer alternative is available. The Section 6(g) authority vitiates the need to address the safety of alternatives during the risk evaluation process.

EPA's proposal may also be counterproductive in some cases. If EPA chose not to make an unreasonable risk finding because of lack of available substitutes, EPA would merely perpetuate the status quo indefinitely, leaving both the toxic chemical and the toxic substitutes on the market. Such a result is not consistent with EPA's mandate under the revised TSCA. The better choice would be to render the unreasonable risk determination and use the subsequent risk management rules to leverage change in product formulations.[37] The Agency would then be in a position to use its effective date and exemption authorities to secure industry commitments on alternatives development and deployment.

Lastly, EPA is required to conduct risk evaluations and reach determinations "without consideration of costs or other non-risk factors," under Section 6(b)(4)(A) of TSCA. Since the risk determination is rendered for the particular chemical(s) under evaluation, consideration of chemicals not covered within the chemical or category designation is a non-risk factor for the chemical(s) in question, and thus prohibited under the revised statute.

In summary, EPA has ample authorities to address the problem of availability of alternatives, if and when it arises, in the risk management decision-making process. The issue is best addressed at that stage, when the "unreasonable risk" conditions of use and associated exposures are known, the alternatives information is current, and the Agency can leverage its available authorities to effect changes in product formulation.

[37] EPA could include both the candidate chemical and the toxic substitutes as a category designation, based upon similarities in use, under Section 26(c) of TSCA. This approach would be particularly useful where there are both safe and unsafe alternatives, and EPA seeks to promote the use of the safe alternatives.

2. Suggestions for EPA's Proposal

Risk Evaluation Process

2(a) EPA's proposal for public comment periods is appropriate; NRDC suggests 90 day comment periods to allow sufficient opportunity for stakeholder comment.

Two of the themes struck by many stakeholders throughout the legislative process that led to enactment of the Frank R. Lautenberg Chemical Safety Act were the need for transparency about how the EPA was making decisions related to implementation, and the importance of the Agency providing opportunities for public input, including via public comment periods prior to many key steps in the implementation process. Indeed, as versions of the legislation were debated and negotiated, Congress added provisions specifying an opportunity for public comment during key steps in the implementation process (for example, in response to a proposed designation of a chemical as "low priority").

Unfortunately, over the years, the industry has developed into an art form calls for excessive rounds of public comment, peer review, and consideration of new studies, successfully slowing agency efforts to a crawl if not a complete standstill.[38] This strategic stalling approach has already begun under TSCA implementation as the chemical industry has sought to delay the proposed rulemakings to ban particular uses of the toxic solvent trichloroethylene ("TCE"); ostensibly to wait for the latest industry-funded study that the solvent manufacturers cannily predict will support its arguments against the need for regulation.

Authoritative bodies including the National Academy of Sciences and the Government Accountability Office have identified the problem of assessments being delayed for years, hindering EPA programs and preventing necessary safeguards from being adopted.[39]

Thus, in establishing the "ground rules" for risk evaluation (as well as prioritization and scoping), it is important that EPA strike the right balance between ensuring sufficient opportunity for input from the public, and setting (and sticking to) clear deadlines after which the Agency will move forward with its process to meet the mandatory, enforceable deadlines established under the law.

In its proposed risk evaluation rule, EPA sets forth an approach for taking public comment during key steps of the implementation process, while also establishing a rule that will prevent the presentation of information that was available during the public comment period but was not submitted to EPA from being used as the basis for challenging EPA's final decisions. The proposal appears intended to establish bright lines for when information must be provided to the Agency for consideration in its process, while allowing EPA to meet the statutory deadlines established by Congress.

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[38] See for example the case studies provided in NRDC's report The Delay Game, which chronicles the decades-long effort of EPA's IRIS Program to complete hazard assessments of TCE, formaldehyde and styrene.

[39] National Research Council, 2009. Science and Decisions: Advancing Risk Assessment, Washington, D.C.: National Academies Press. pp.3, 17, 45-46. Available at: https://www.nap.edu/catalog/12209/science-and-decisions-advancing-risk-assessment; Government Accountability Office, "Toxic Chemicals: EPA's New Assessment Process Will Increase Challenges EPA Faces in Evaluating and Regulating Chemicals" (April 29, 2008)

In concept, NRDC supports EPA's proposed approach, assuming certain precedent steps that have been proposed in the process are fully met. The risk evaluation rule is part of a multi-step process established under the revised law that includes prioritization to identify high-risk chemicals for evaluation, and a scoping process to identify all known, intended, or reasonably foreseeable uses. In its proposed prioritization rule, EPA outlines plans to gather data and information on chemicals as part of a pre-prioritization step, to ensure that once chemicals are taken up in the prioritization process, much of the information needed to prioritize and potentially evaluate a chemical has already been collected.

NRDC supports this approach to getting an early start on gathering information on chemicals that may be taken up in the prioritization process – including the Agency's use of its own authorities under TSCA sections 4, 8 and 11. EPA has also proposed to include public comment periods as part of the scoping process, prioritization process and risk evaluation process, including in at least one instance where a public comment period is not mandated under the new law. NRDC supports the inclusion of public comments at each of the steps proposed by EPA. Assuming that the rest of EPA's prioritization and risk evaluation rules are finalized along the lines of the proposals, with early efforts to gather information on chemical substances and opportunities for public comment, NRDC supports the approach outlined by EPA: establishing deadlines for the draft risk evaluation, after which introduction of "all comments that could be raised on the matters addressed and issues presented in the draft risk evaluation" but that were not raised "may not form the basis for an objection or challenge in any subsequent administrative or judicial proceeding."

In its proposed risk evaluation rule, EPA asks for comment on "whether and how the proposed rule could provide additional transparency, public accountability, opportunities for public participation, or incorporation of statutory deadlines."[40] Although the law sets a minimum window for comments of "at least 30 days," realistically all stakeholders will need more time to be able to participate meaningfully and constructively in the process. NRDC recommends that EPA provide 90-day comment periods to allow the public sufficient time to absorb and develop comments on draft evaluations, including evaluations of substances nominated for consideration by the chemical industry pursuant to [Section 6(4)(C)(ii)]. In most instances, 90 days will allow sufficient time to comment while not derailing the Agency from fulfilling its obligations within the statutory deadlines.

Lastly, in its Proposed Section 702.47, EPA lists the materials that will be included in the public docket for each risk evaluation.[41] Public comments received by the Agency regarding the proposed risk evaluation should also be included in the docket. While this may be EPA's intent, it should be explicitly stated and clarified in the final rule.

2(b) EPA should require substantiation of all non-exempt Confidential Business Information claims.

EPA's proposed risk evaluation rule will require manufacturers requesting risk evaluations of chemicals to submit upfront substantiation for non-exempt Confidential Business Information ("CBI") claims and to certify that any such claims of confidentiality are true and correct. NRDC supports this proposed approach, and further recommends that in its final rule EPA clarify in the preamble that upfront

[40] 82 Fed. Reg. 7565
[41] 82 Fed. Reg. 7580

substantiation is required for all non-exempt CBI claims made in response to EPA information requests for any chemical that undergoes risk evaluation, not just the "industry-requested" chemicals. This is another important means by which EPA can "provide additional transparency, public accountability, [and] opportunities for public participation." [42]

2(c) EPA should initiate interagency collaborations with states as part of risk evaluations.

NRDC agrees that the existing mechanisms for initiating interagency collaboration are sufficient; not codifying a specific process affords EPA the flexibility needed to initiate the most effective collaborations and do so in a timely manner. However, it is important that interagency consultation measures be described in the draft scope document for transparency, and to enable stakeholders to identify additional agencies that may have relevant information as needed.

Collaboration with other agencies is essential because EPA will need to comprehensively understand the conditions of use for chemicals. The Federal Register notice mentions The National Institute for Occupational Safety and Health ("NIOSH") and Occupational Safety and Health Administration ("OSHA"); we agree these agencies will be important sources of information about workers. Additionally, the Food and Drug Administration ("FDA"), the Consumer Product Safety Commission ("CPSC") and the Centers for Disease Control and Prevention ("CDC") will likely have important data biomonitoring studies and chemicals in food and consumer products.

EPA should also include state agencies as potential partners for interagency consultation. State agencies can provide valuable information on multiple aspects of a risk evaluation, including conditions of use, susceptible populations, and exposures. A number of states including Washington,[43] Vermont,[44] and Maine[45] have laws requiring reporting of certain hazardous chemicals used in products. The Massachusetts Toxics Use Reduction Act ("TURA") requires Massachusetts companies that use large quantities of specific toxic chemicals to evaluate and plan for pollution prevention opportunities, implement them if practical, and annually measure and report the results.[46] California Environmental Protection Agency ("CalEPA") implements a number of relevant state programs, including California's landmark right-to-know law on hazardous chemicals in products, known as "Proposition 65,"[47] as well as the Safer Consumer Products Program.[48] The California Department of Public Health[49] Safe Cosmetics Program, Occupational Health and Evaluation program and others could also be valuable sources. Other states doubtless have programs and data like these, and more, that can inform EPA's evaluations. In addition, state poison control centers may have relevant reports. Drawing upon the extensive

[42] 82 Fed. Reg. 7565
[43] WA Children's Safe Product Act: http://www.ecy.wa.gov/programs/hwtr/RTT/cspa/
[44] VT Chemical Disclosure Program for Children's Products: http://healthvermont.gov/environment/children/chemicals-childrens-products
[45] ME Safer Chemicals in Children's Products: http://www.maine.gov/dep/safechem/
[46] http://www.mass.gov/eea/agencies/massdep/toxics/tur/
[47] CA Safe Drinking Water and Toxic Enforcement Act of 1986: https://oehha.ca.gov/proposition-65
[48] CA Safer Consumer Products Program: http://www.dtsc.ca.gov/SCP/index.cfm
[49] CA Department of Public Health, Occupational Health Branch Programs: https://www.cdph.ca.gov/programs/ohb/Pages/Programs.aspx

experience of states will be a critical aspect of ensuring an effective partnership between states and EPA.

2(d) The description of the scoping document is broad enough to include relevant guidances, peer review plans, and interagency consultations; it would be helpful to list these items explicitly.

NRDC agrees that the scope of the risk evaluation must identify the hazards, exposures, conditions of use, and the potentially exposed or susceptible subpopulations the Administrator expects to consider, as required by § 2605 (b)(4)(D). We also support EPA's proposal to include in the scope of the risk evaluation other information that the agency intends to rely upon: ecological characteristics; the reasonably available information, science policies, models, and screening methodologies that EPA plans to use; the conceptual model that articulates the relationship between the chemical substance and human and environmental receptors; and the analysis plan that identifies the approaches, methods and metrics to be used as well as the strategy for using information and accepted science policies, models, and screening methodologies. These elements are essential for a risk evaluation that addresses the risk of injury to health and the environment, as required by statute. Including this information is also necessary for facilitating informed and meaningful public comment and ensuring that the information that EPA considers in the risk evaluation is complete. In the same spirit, in response to EPA's query, 82 Fed. Reg. 7573 3/3, we urge EPA to explicitly require for each risk evaluation that a list of appropriate guidance documents to be relied upon be included in the scoping document for public review and comment.

In addition, as discussed elsewhere in these comments, the revised TSCA requires EPA to evaluate relevant aggregate exposures to potentially exposed or susceptible populations when rendering risk evaluation determinations. Accordingly, NRDC fully expects the Analysis Plan in the scoping documents, as proposed in 40 CFR 702.39(c)(5), to expressly identify the aggregate exposure scenarios EPA intends to assess in a chemical's risk evaluation. The pre-prioritization process and the draft scoping document comment period would enable the public to identify the conditions of use and aggregate exposure scenarios warranting evaluation, in anticipation of the final scoping document.

We also note some discrepancies between the discussion of this section in the preamble and the proposed regulatory text. First, at 82 Fed. Reg. 7572 & 73, EPA explains in the preamble that it intends to identify peer review plans and include those plans in the scope document. Similarly, EPA states intent to document interagency consultations in the scope document.[50] NRDC supports both these proposals to facilitate public comment on the peer review plans and the planned interagency consultations respectively. However, the proposed regulations do not explicitly reference the documentation of peer review plans or interagency consultations.[51] EPA should clarify the proposed regulatory language to be consistent with the proposal preamble by adding a reference to both peer review plans and interagency consultations in the list of items to be included in the scope document. While the Analysis Plan outlined in Proposed § 702.39(c) is theoretically broad enough to encompass the documentation of both peer review plans and interagency consultations, explicitly identifying these items for inclusion will ensure

[50] 82 Fed. Reg. 7568
[51] *See* Proposed § 702.39(c)

that they are always considered and included, as the preamble language indicates.

Second, the preamble states that EPA plans to provide a 45 calendar day public comment period on the draft scope document, 82 Fed. Reg. 7570, but the proposed regulation mentions only a 30 day comment period, *see* Proposed § 702.39(c)(6)(ii). Given that the scoping document will define the shape of the risk evaluation to follow and that it will cover significant ground, NRDC supports the 45 day comment period, especially since issues that could be raised at this stage are considered waived if they are not raised. EPA should update the proposed regulatory language to reflect the preamble and provide a 45 day comment period.

2(e) NRDC supports EPA's proposal that all draft risk evaluations undergo peer review; low priority and no unreasonable risk findings should also undergo peer review.

NRDC agrees with EPA that all risk evaluations must be peer reviewed, per proposed 40 CFR 702.41(c). In its final rule, the Agency should clarify that risk evaluations conducted pursuant to manufacturer requests will also undergo peer review, per proposed 40 CFR 702.37(e)(7).[52] Risk evaluations submitted to the Agency by chemical manufacturers or other interested parties, pursuant to section 26(l)(5) should also undergo peer review.

EPA recognizes the importance of setting high standards for peer review if it is to ensure a credible and publicly acceptable product. The Proposed Rule states that EPA will conduct its peer reviews according to the guidances provided in the OMB Peer Review Bulletin[53] and the EPA Peer Review Handbook (2015), which also cover contractor-managed peer reviews.[54] (Note that the reference #23 in the Proposed Rule is to the 3rd Edition (2006), and not the 4th Edition (2015) of the Peer Review Handbook – this should be updated).

NRDC agrees with the Proposed Rule that the Agency needs some flexibility in selecting the type and level of peer review that is appropriate for different situations. NRDC recognizes that there are different kinds of peer review to serve different purposes, as discussed in the preamble to the OMB Peer Review Bulletin[55] and the EPA Peer Review Handbook, 4th Edition (2015).[56] Examples of peer reviewers could include internal review by EPA staff not involved with the product under review, inter-agency review, or review by external parties outside the federal agencies.

If the goal is to gather scientific or technical feedback, then EPA must ensure that individuals and panels

[52] "(7) No preferential treatment. EPA will not expedite or otherwise provide special treatment to a risk evaluation conducted as a result of a manufacturer request."

[53] OMB. 2004. Final Information Quality Bulletin for Peer Review. http://www.whitehouse.gov/sites/default/files/omb/memoranda/fy2005/m05-03.pdf

[54] EPA 2015. Peer Review Handbook 4th Edition. https://www.epa.gov/osa/peer-review-handbook-4th-edition-2015

[55] OMB. 2004. Memorandum for Heads of Departments and Agencies, *Final Information Quality Bulletin for Peer Review*. http://www.whitehouse.gov/sites/default/files/omb/memoranda/fy2005/m05-03.pdf

[56] EPA 2015. Peer Review Handbook 4th Edition. https://www.epa.gov/osa/peer-review-handbook-4th-edition-2015

are free of actual or potential financial conflicts and competing interests, and that there is not an appearance of bias or lack of impartiality.

If EPA uses a contractor-managed peer review process, the EPA Peer Review Handbook provides for a direct interaction between EPA and the contractor in addressing actual or potential conflicts of reviewers, including having the contractor consult directly with the EPA Science Advisor (Handbook, p. 59-60). Any competing interests of the contractor should also be publicly disclosed; contractors with financial conflicts should be avoided (Handbook, Section 4.6.5). In particular, organizational conflicts that may bias a contractor's judgment should be avoided.

EPA may want to gather feedback from stakeholders representing various interests, including stakeholders with financial and competing interests. If this is the case, EPA must be transparent about what position stakeholders are representing and require full public disclosure of competing (financial and non-financial) interests. For example, industry input on technical questions including industry practices can be very valuable, but should be gathered through a public process with public disclosure of financial conflicts and competing interests.

NRDC strongly disagrees with the examples given in the preamble of when peer review might not be needed for a risk evaluation: "where a chemical substance is found to not present an unreasonable risk or that findings are similar or the same as other jurisdictions (states or countries) that have reached similar conclusions on the same information, such that the Agency could determine that peer review is not necessary for that chemical risk evaluation."[57]

Determinations that a chemical does not pose an unreasonable risk must also undergo peer review, because of the potential public impact and public interest in declaring chemicals as "low priority," or low or no risk. In fact, the potential health and environmental impacts of making an error in such an assessment – that is, a "false negative" – could be devastating. NRDC believes that assessments that result in reducing hazard classifications are definitely also in need of public comment and transparent rigorous peer review.

An example of both the public interest and public impact of classifying chemicals as low or no risk is the controversial FDA program that declares food additives as Generally Regarded as Safe ("GRAS") without public input or independent peer review. In June, 2015 FDA was petitioned to ban eight chemical flavorings, found in ice cream, baked goods, candy, and beverages, that cause cancer in lab animals.[58] The petition was filed by NRDC, the Center for Science in the Public Interest, the Center for Food Safety, Consumers Union, Improving Kids' Environment, Center for Environmental Health, and the Environmental Working Group – representing millions of Americans.[59] The International Agency for Research on Cancer ("IARC"), an arm of the World Health Organization, designates five of the synthetic flavorings as causing cancer in animals and "possibly carcinogenic to humans," and the Office of Environmental Health Hazard Assessment ("OEHHA") in California designates seven of them as

[57] 82 Fed. Reg.7573

[58] The full petition is here: https://www.nrdc.org/resources/nrdc-others-file-petition-asking-fda-ban-eight-carcinogenic-flavorings

[59] Press Release. June 10, 2015. NRDC, Others Petition FDA to Ban Eight Carcinogenic Flavorings in Food. https://www.nrdc.org/media/2015/150610

carcinogens. A public report by Pew Charitable Trusts has called the FDA food additive regulatory system "plagued with systemic problems, which prevent the agency from ensuring that their use is safe" and specifically identified the GRAS program as marred by potential conflicts of interest.[60] If the EPA TSCA program acts similarly to the FDA GRAS program by declaring chemicals as "safe" (low priority, low risk, no risk, etc.) without independent public peer review it will erode public trust in the whole TSCA program and EPA, and could lead to a similar failure to protect the public from exposure to unsafe chemicals.

Even if EPA is affirming a previous evaluation that a chemical is low priority or low/no risk, EPA should solicit public comment and an independent transparent peer review if there is any new data or new information that could affect the evaluation. For example, recently EPA completed an internal assessment of the potential carcinogenicity of glyphosate, the most widely used pesticide on the market and the main ingredient in Monsanto's RoundUp products. EPA had not planned to issue its cancer assessment for public comment or peer review because it did not change the previous determination that it was "not likely to be carcinogenic to humans." (CARC, 2015, TXR #0057299)[61] Given that there were additional new data available since the previous assessment, and that the International Agency for Research on Cancer had earlier that year listed it as "probably carcinogenic to humans" (Group 2A; IARC 2015), EPA's failure to have its "no risk" decision peer reviewed caused a global public outcry, intense media coverage,[62] and the convening of a new Scientific Advisory Panel in December, 2016.[63] Clearly a declaration that a chemical has no cancer risk is of great public interest, and making that declaration without a public and transparent peer review process resulted in a discredited evaluation and eroded trust in EPA.

NRDC also disagrees that risk assessments from other jurisdictions may not need peer review (where "findings are similar or the same as other jurisdictions (states or countries) that have reached similar conclusions based on the same information."[64]) Other jurisdictions operate under their own particular statutes and regulations, and may not require the consideration and protection of vulnerable populations to the extent that TSCA does. Further, TSCA requires that determinations of unreasonable risk be made without any consideration of cost or other non-risk factors, which may not be the case in other jurisdictions. Finally, neither the EPA Peer Review Handbook nor the OMB Bulletin recognize a category of exemptions from peer review for risk assessments from other jurisdictions as described by

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[60] The Pew Charitable Trusts. Food Additives Project. http://www.pewtrusts.org/en/archived-projects/food-additives-project

The Pew Charitable Trusts. (2013) Issue Brief: Workshop on Potential Conflicts of Interest in GRAS Additive Decisions. http://www.pewtrusts.org/en/research-and-analysis/issue-briefs/2013/08/14/workshop-on-potential-conflicts-of-interest-in-gras-additive-decisions

[61] EPA 2016. Glyphosate Issue Paper: Evaluation of Carcinogenic Potential, EPA's Office of Pesticide Programs, https://www.epa.gov/sites/production/files/2016-09/documents/glyphosate_issue_paper_evaluation_of_carcincogenic_potential.pdf

Reuters May 2, 2016. EPA takes offline report that says glyphosate not likely carcinogenic. http://www.reuters.com/article/us-usa-glyphosate-epa-idUSKCN0XU01K

[62] Reuters May 2, 2016. EPA takes offline report that says glyphosate not likely carcinogenic. http://www.reuters.com/article/us-usa-glyphosate-epa-idUSKCN0XU01K

[63] Glyphosate SAP information available at Docket ID EPA-HQ-OPP-2016-0385-0495 and on the SAP website at: https://www.epa.gov/sap/meeting-materials-december-13-16-2016-scientific-advisory-panel

[64] 82 Fed. Reg. 7573

EPA in the preamble to its proposed rule. As discussed above, there are different types and levels of peer review options, and assessments from other jurisdictions should at a minimum undergo some level of internal Agency peer review.

The proposed rule specifically requests comment on whether there are circumstances where peer review may not be warranted.[65] NRDC agrees that a separate peer review may not be warranted for an individual component of a risk evaluation, such as a hazard assessment. For example, where authoritative bodies such IARC, the National Institute of Environmental Health Sciences ("NIEHS") National Toxicology Program ("NTP"), or EPA's Integrated Risk Information System ("IRIS") has performed a hazard assessment, a separate peer review of the hazard assessment is unnecessary. NRDC believes that once such a hazard assessment is incorporated into a risk evaluation, that risk evaluation *should* undergo peer review.

In conclusion, risk evaluations are the foundation of the TSCA regulatory program, and the rigorous public scrutiny, oversight, and accountability that a well-conducted independent transparent peer review provides is essential, regardless of the generating entity or whether the evaluation finds an unreasonable risk.

2(f) Other needed clarifications.

2(f)(i) Reducing use of vertebrate animals.

In its proposed rule Sec. 702.39(b)(5), EPA states that, "where appropriate, to the extent practicable, and scientifically justified, EPA will use information generated without the use of testing on vertebrates in performing risk evaluation."[66]

To be consistent with the statute, EPA's statement should be revised to say:

"where appropriate, to the extent practicable, ~~and~~ scientifically justified, and consistent with the policies of Title 1 of the law, EPA will use information generated without the use of testing on vertebrates in performing risk evaluation."

In addition, consistent with TSCA section 4(h)(2)(C), EPA should clarify in the final rule that the information generated without the use of testing on vertebrates must be "scientifically reliable, relevant, and capable of providing information of equivalent or better scientific reliability and quality to that which would be obtained from vertebrate animal testing."

[65] 82 Fed. Reg. 7573
[66] 82 Fed. Reg. 7578

Risk Evaluation Components

2(g) NRDC agrees that EPA's proposed risk evaluation process generally reflects appropriate systematic review approaches.

NRDC appreciates that EPA has specifically elevated the systematic review approach adopted by NTP of the NIEHS. The NTP method is well-described, has undergone extensive peer review and public comment, and has been used successfully in an increasing number of cases, proving its utility and value.[67, 68] The NTP systematic review provides a sturdy and practical framework – simple, functional, and effective - for enhancing transparency and communication, promoting consistency, and facilitating reproducibility across literature-based evaluations of hazardous chemicals. NRDC offers the following general commentary on how systematic review should be implemented at EPA.

Assessing study quality – EPA's Proposed Rule mentions one element of evaluating the quality of the body of evidence- the risk of bias (internal study validity, one element of evaluating the quality of the body of evidence), and goes on at some length praising studies that are conducted according to Organisation for Economic Co-operation and Development ("OECD") guidelines, EPA test guidelines, and Good Laboratory Practices ("GLP"). NRDC disagrees that these are appropriate measures of study quality. Guideline and GLP studies – mostly sponsored by industry to meet regulatory requirements - don't necessarily use modern methods for evaluating chemicals and are not designed to grapple with the problems of low-dose exposures, complex and systemic endocrine effects, behavioral or learning effects, metabolic perturbations, or upstream effects like reduced sperm count or reduced anogenital distance which are predictors of infertility. Furthermore, GLP and Guideline studies are not consistently associated with higher quality research, proper study design or correct statistical analysis.[69, 70] Relying on the inappropriate assumption that GLP and Guideline studies are high quality and that all other studies are not will bias against the consideration of results from academic studies, including those funded by government agencies. This is an inappropriate and unsupported delineation of the reliability and validity of scientific findings that ignores other critical factors such as independent replication, use of appropriate and sensitive state-of-the-science techniques, and peer-review of the evidence. GLP and Guideline studies rarely satisfy these criteria. Instead of assuming that these types of studies are high-quality evidence, EPA should outline the criteria by which scientific evidence will be evaluated for internal and external validity, including a process by which non peer-reviewed studies (such as GLP and Guideline studies) will undergo review as part of the systematic review process. EPA has a number of different mechanisms by which this could be accomplished, for example by eliciting two independent unconflicted reviewers or a panel of experts to peer-review the scientific findings.

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[67] NTP Systematic Review. https://ntp.niehs.nih.gov/pubhealth/hat/noms/index-2.html

[68] Rooney AA, Boyles AL, Wolfe MS, Bucher JR, Thayer KA. 2014. Systematic review and evidence integration for literature-based environmental health science assessments. Environ Health Perspect 122:711–718

[69] Myers, J. P., F. S. vom Saal, et al. (2009). "Why public health agencies cannot depend on good laboratory practices as a criterion for selecting data: the case of bisphenol A." Environ Health Perspect 117 (3): 309-15.

[70] Vandenberg LN, Ågerstrand M, Beronius A, Beausoleil C, Bergman Å, Bero LA, Bornehag CG, Boyer CS, Cooper GS, Cotgreave I, Gee D, Grandjean P, Guyton KZ, Hass U, Heindel JJ, Jobling S, Kidd KA, Kortenkamp A, Macleod MR, Martin OV, Norinder U, Scheringer M, Thayer KA, Toppari J, Whaley P, Woodruff TJ, Rudén C. A proposed framework for the systematic review and integrated assessment (SYRINA) of endocrine disrupting chemicals. Environ Health. 2016 Jul 14;15(1):74.

As an example, for assessing the quality of individual studies the NTP framework evaluates the risk of outcome-specific bias using five domains: selection bias, performance bias, attrition bias, detection bias, and reporting bias. This approach is a great improvement over simple reporting quality – which biases towards GLP and guideline studies - as a proxy for study quality. In addition to including a consideration of these sources of potential bias, EPA should include funding bias. It is well documented and generally accepted that financial sponsorship (i.e. source of funding) introduces a risk of bias on the results and conclusions in favor of the regulated industry's interests.[71, 72, 73, 74] Recognizing this, medical study review committees have proposed including conflict of interest considerations as an independent item when assessing bias in clinical studies.[75] Toxicologists have made similar recommendations, and other frameworks for systematic review of environmental health evidence have incorporated extracting information regarding study funding source as part of the review process. [76, 77, 78, 79]

Interpreting negative data – In its Proposed Rule EPA mentions, "integrating negative data (and consideration of the quality of those data)…" without providing any guidance. The NTP systematic review approach is to exclude negative data (null studies) that are inconsistent across studies, when the underpowered studies are showing null association. This is because an underpowered study that fails to find an effect (negative data) cannot be interpreted as demonstrating that there is no effect—the study may not be adequately powered to demonstrate an effect, even if one truly exists. However, an underpowered study that does find an effect (positive data) should not necessarily be excluded, particularly if it is consistent with findings in other studies because if the study was able to detect an effect even when underpowered this should increase the confidence that a true effect exists. This issue is particularly relevant to epidemiologic studies, which may be underpowered, for example due to poor exposure information, small cohort size, short exposure duration, or when not enough time has passed since the exposure (inadequate latency).

Additional publically available information - For selecting information at the start of a systematic review,

[71] Mandrioli D, Silbergeld EK. Evidence from Toxicology: The Most Essential Science for Prevention. Environmental Health Perspectives. 2016;124(1):6-11.

[72] Lundh A, Sismondo S, Lexchin J, Busuioc OA, Bero L. 2012. Industry sponsorship and research outcome. Cochrane Database Syst Rev 12:MR000033

[73] Bero L, Oostvogel F, Bacchetti P, Lee K. 2007. Factors associated with findings of published trials of drug–drug comparisons: why some statins appear more efficacious than others. PLoS Med 4:e184

[74] Barnes DE, Bero LA. 1998. Why review articles on the health effects of passive smoking reach different conclusions. JAMA 279:1566–1570.

[75] Bero LA. 2013. Why the Cochrane risk of bias tool should include funding source as a standard item [Editorial]. Cochrane Database Syst Rev 12

[76] Neltner TG, Alger HM, O'Reilly JT, Krimsky S, Bero LA, Maffini MV. 2013. Conflicts of interest in approvals of additives to food determined to be generally recognized as safe: out of balance. JAMA Intern Med 173:2032–2036.

[77] Mandrioli D, Silbergeld EK. Evidence from Toxicology: The Most Essential Science for Prevention. Environmental Health Perspectives. 2016;124(1):6-11.

[78] Woodruff TJ, Sutton P. 2014. The Navigation Guide systematic review methodology: a rigorous and transparent method for translating environmental health science into better health outcomes. Environ Health Perspect 122:1007–1014

[79] Rooney AA, Boyles AL, Wolfe MS, Bucher JR, Thayer KA. Systematic review and evidence integration for literature-based environmental health science assessments. Environ Health Perspect. 2014 Jul;122(7):711-8

NRDC supports being as comprehensive as reasonably possible by gathering the published, unpublished, and "grey" literature (publicly available government reports, etc.) as part of the literature search. It is appropriate to be as comprehensive as possible in gathering all the available data as a first step. These data can then be reviewed internally according to a systematic review framework like the NTP method.

2(h) EPA should rely on current, up-to-date guidance for risk assessment.

It is appropriate for EPA to review and utilize existing guidance documents when the existing documents are relevant, up-to-date, and specific enough to provide the appropriate frameworks and resources needed to guide the risk evaluation. However, the compendium EPA references in the preamble[80] contain a number of guidelines which do not reflect scientific advances in exposure assessment and toxicology.

The Guidelines for Exposure Assessment are nearly 25 years old, and EPA's update to these Guidelines (hereafter referred to as the "Draft Exposure Guidelines") underwent public comment and expert peer review in 2016. The Draft Exposure Guidelines identified multiple ways in which the field of exposure science has significantly "expanded and changed."[81] These advances include methods for assessing aggregate exposure and vulnerable populations:

> "The exposure science field has evolved to recognize the contribution of individual characteristics and activities to exposure, recognizing that not all individuals are alike, behave the same way or are exposed to the same concentration of a chemical."
>
> "Models that consider multipathway, multiroute exposures and apply probabilistic methods to simulate behavior patterns have advanced in recent years. Improvements in monitoring methodology and modeling now enable some exposure analyses and assessments to consider the influences of age, sex, culture, ethnicity, activity patterns and socioeconomic and demographic factors."[82]

It would therefore be inappropriate for EPA to rely on the 1992 version of the Exposure Guidelines as a basis for risk evaluations.

Similarly, the science describing early-life vulnerability to carcinogens has advanced since EPA published the 2005 Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens. For example, as discussed in more detail in Section 3(h) on defaults and uncertainty factors, the OEHHA guidance for incorporating differential susceptibilities to carcinogens and non-carcinogens incorporates more recent science on increased susceptibility during the prenatal period and age-related susceptibility for non-mutagenic carcinogenic agents.[83, 84] Since the 2005 Guidance does not include these methods

[80] 82 Fed. Reg. 7570

[81] USEPA 2016. Guidelines for Human Exposure Assessment. Risk Assessment Forum, Peer Review Draft p.20. https://www.epa.gov/sites/production/files/2016-02/documents/guidelines_for_human_exposure_assessment_peer_review_draftv2.pdf

[82] Id. p.21

[83] California EPA 2009. Cal EPA 2009. California Environmental Protection Agency, Office of Environmental Health Hazard Assessment. Technical Support Document for Cancer Potency Factors: Methodologies for derivation,

for accounting for early-life susceptibility, reliance on the 2005 Guidance to evaluate cancer risk would underestimate risk for vulnerable populations.

Where existing EPA guidance is out-of-date or incomplete, EPA should look to other scientifically valid resources and guidance documents from federal and state agencies, peer-reviewed literature, and National Academy of Sciences ("NAS") reports, most notably 2009's *Science and Decisions: Advancing Risk Assessment* (hereafter referred to as "*Science and Decisions*").[85]

Advances in exposure science, as described in EPA's Draft Exposure Guidelines, support the need to ensure that exposure assessments carefully examine the potential for increased susceptibility of any individual/lifestage/group/population, which may require, "a dialogue with toxicologists/health scientists to consider whether a specific 'window of susceptibility' during a given lifestage is important to a particular risk assessment."[86] To ensure that this science is reflected in the risk evaluation process, we urge EPA to clarify in the preamble that the list of information specifically identified in 702.39 (e) (4) (i-iv) would include the following in order to ensure comprehensive exposure assessments for vulnerable populations:

- Data, and/or models, which describe the conditions that lead to the highest concentrations and resulting exposures and those situations that lead to exposure for the most susceptible individual/lifestage/group/population.

2 (i) EPA should clarify the definitions of "sentinel exposure" and "routes of exposure."

2(i)(i) Aggregate and Sentinel Exposures.

In the scoping phase of the risk evaluation, EPA must review all of the known, intended or reasonably anticipated uses of a chemical and identify all exposure pathways for each of the potentially exposed subpopulations. From this analysis, EPA will identify the exposure(s) of greatest concern for the most susceptible population. Because aggregate exposures to vulnerable populations reflect real-world situations[87] and the harmful effects of exposure to chemicals can result from the totality of exposures from multiple pathways,[88] the presumption in the scoping phase should be to evaluate the potential significance of all routes and pathways for exposure, from all uses.

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listing of available values, and adjustments to allow for early life stage exposures. http://oehha.ca.gov/media/downloads/crnr/tsdcancerpotency.pdf

[84] Cal EPA 2008. California Environmental Protection Agency, Office of Environmental Health Hazard Assessment. Technical Support Document For the Derivation of Noncancer Reference Exposure Levels http://oehha.ca.gov/media/downloads/crnr/noncancertsdfinal.pdf

[85] National Research Council, 2009. Science and Decisions: Advancing Risk Assessment, Washington, D.C.: National Academies Press.

[86] USEPA 2016. Guidelines for Human Exposure Assessment. Risk Assessment Forum, Peer Review Draft. p.34

[87] Id. p.16

[88] National Research Council. 1993. Pesticides in the Diet of Infants and Children.

This scientific need for aggregate exposure evaluation is consistent with the statutory mandate to conduct aggregate exposure analyses, where relevant. As indicated in the conditions of use section above, the aggregate exposure evaluation obligation is derived from the broad statutory definition of conditions of use, the definition of "potentially exposed or susceptible populations," the mandatory consideration of combinations of activities in reaching unreasonable risk determinations, and the mandatory consideration of the duration, intensity, frequency, and number of exposures in reaching these risk determinations. Accordingly, as both a legal and technical matter, consideration of aggregate exposure is necessary and appropriate for the vast majority of evaluations.

Nevertheless, as discussed below, where there is evidence that an exposure may serve as a warning for other exposures - and removing the harmful "sentinel" exposure is indicative of reduced risk to related exposures - a sentinel exposure approach may be warranted for the risk evaluation. We expect these instances to be relatively infrequent, and thus the definition of sentinel is considered in this context.

EPA rightly notes that the term "sentinel exposure" is a term not previously used by EPA in the context of exposure assessment, or risk evaluation. In fact, the phrase is not found in EPA's recent Draft Exposure Guidelines which focuses on the terminology well established in exposure science - "single chemical and single pathway," "aggregate," and "cumulative."[89] However, the term "sentinel" is used by other federal agencies charged with protecting public health. Accordingly, EPA must ensure that the definition of "sentinel exposure," in proposed rule 40 CFR 702.33, is clear and consistent with other relevant uses of the term "sentinel" in occupational health and public health surveillance. For the reasons discussed below, EPA's proposed definition requires further clarification to be consistent with these established meanings.

Occupational health and infectious disease surveillance utilizes the concept of sentinel health events to identify opportunities for public health interventions to prevent widespread morbidity and mortality. [90] The concept originated with the publication of a list of health events defined as "a preventable disease, disability, or untimely death whose occurrence serves as a warning signal that the quality of preventive and/or therapeutic medical care may need to be improved."[91] Surveillance systems built on this concept are defined by CDC as those which collect information from a limited set of sites chosen as indicators of threats to the larger population.[92] Therefore interventions which address the "sentinel event" will prevent or lessen the impact on the broader population, and health impacts in the general population should not rise in the absence of the sentinel event.

In a context more analogous to chemical risk evaluation, NIOSH adapted the concept of sentinel events as a "warning signal" to occupational medicine and defined Occupational Sentinel Health Events as "an event whose occurrence may serve as a warning signal that materials substitution, engineering control, personal protection, or medical care may be required."[93] The implementation of any of these measures

[89] USEPA 2016. Guidelines for Human Exposure Assessment. Risk Assessment Forum, Peer Review Draft. p.16
[90] Rabinowitz. et al 2009. Human and Animal Sentinels for Shared Health Risks. Vet Ital. 2009 ; 45(1): 23–24.
[91] NIOSH. 2011. OCCUPATIONAL SENTINEL HEALTH EVENTS SHE(O); https://www.cdc.gov/niosh/topics/sheo/
[92] Centers for Disease Control and Prevention. Lexicon, Definitions, and Conceptual Framework for Public Health Surveillance.. MMWR 2012;61(Suppl; July 27, 2012):pp10--14. https://www.cdc.gov/mmwr/preview/mmwrhtml/su6103a3.htm
[93] NIOSH. 2011. OCCUPATIONAL SENTINEL HEALTH EVENTS SHE(O); https://www.cdc.gov/niosh/topics/sheo/

would therefore prevent further disease or disability. For example, the NIOSH Sentinel Event Notification System for Occupational Risk ("SENSOR") program supports surveillance of acute pesticide illnesses in key states to identify emerging pesticide problems which has led to improvements in training, personal protective equipment, and application methods to prevent pesticide-related disease.[94]

In these contexts, it is critical that the sentinel exposure is demonstrated to be a sufficient "warning" for all the potential subpopulations purported to be covered by the exposure pathway(s). It is this demonstration element that is missing from the EPA definition as proposed. Accordingly, we suggest clarifying text as follows:

> Sentinel exposure means the exposure(s) of greatest significance, which may be the plausible maximum exposure to an individual, population (or subpopulation), or the environment, to the chemical substance of interest (or any combination thereof), <u>demonstrated to be indicative of relevant exposures for all potentially exposed or susceptible subpopulations</u>.

2(i)(ii) Routes of exposure definition.

The definition of "routes" in Section 702.33 should be clarified to remove the word "absorption" because, as EPA is aware, fibers of substances like asbestos can become lodged in tissues or organ linings, causing damage even if they are not fully "absorbed." We suggest the following clarification in the definition, to remove this unintentional error:

"Routes means the particular manner which a chemical substance may contact the body, including ~~absorption~~ via ingestion, inhalation, or dermally (integument)."

2 (j) Data from high throughput assays cannot be used to demonstrate low hazard or exposure.

NRDC offers the following general commentary on the interpretation of data from high throughput assays. High-throughput chemical toxicity testing has been implemented in large-scale agency projects, including the Toxicity Forecaster (ToxCast™) and Tox21 projects at EPA and NIEHS. While some initial data indicate that the methods may have promise,[95] the ability of these methods to accurately predict chemically-induced perturbations at the tissue, whole organism, and population levels remains to be determined. Two recent reports from the National Research Council of the National Academies of Sciences, *Application of Modern Toxicology Approaches for Predicting Acute Chemical Toxicity for*

[94] NIOSH. 2017. PESTICIDE ILLNESS & INJURY SURVEILLANCE. https://www.cdc.gov/niosh/topics/pesticides/overview.html

[95] Huang R, Sakamuru S, Martin MT, Reif DM, Judson RS, Houck KA, et al. Profiling of the Tox21 10K compound library for agonists and antagonists of the estrogen receptor alpha signaling pathway. Sci Rep [Internet]. 2014 Jan;4:5664
Rotroff DM, Martin MT, Dix DJ, Filer DL, Houck KA, Knudsen TB, et al. Predictive endocrine testing in the 21st century using in vitro assays of estrogen receptor signaling responses. Environ Sci Technol [Internet]. 2014 Aug 5;48(15):8706-16

Chemical Defense[96] and *Using 21st Century Science to Improve Risk-Related Evaluations*,[97] both explored the limitations of emerging tools in toxicology for hazard assessment. While advances are occurring rapidly, the lack of biological coverage and complexity, inability to properly assess metabolism, over-reliance on known pathways of toxicity, and unknown relationship between acute and chronic outcomes make the interpretation of results from emerging methods complex. Though negative results should not be used to indicate that a chemical does not pose a hazard, positive results can be used to affirmatively indicate the presence of a particular hazard trait.[98]

Data cannot be used to demonstrate absence of hazard: The limitations highlighted by the National Academies reports demonstrate that interpretation of data from emerging tools is not straightforward. While these tests are useful in demonstrating activity on the receptors or pathways assayed, a lack of response does not show that a chemical or chemical mixture lacks a biological response. Failure to test positive in these screening assays does not mean that a chemical is "safe," non-toxic or even necessarily a "low priority" for a more thorough assessment. For example, studies found that some chemicals known to disrupt steroidogenesis or thyroid did not show these effects in the high-throughput assays.[99] These methods can neither be used to exonerate a test chemical, or dismiss evidence of hazard from reliable whole animal or human data such as animal bioassays, epidemiologic studies, or case reports.

Data can be used to support affirmative hazard determinations: However, these data can be useful to support evidence of hazard/adverse effects from other types of studies including toxicology and epidemiology. Because high-throughput assays are simply traditional *in vitro* and mechanistic tests conducted at a much larger scale, positive results can be used in the same way that positive results from these types of tests have always been used—as a parallel stream of data to support hazard trait assignments and/ or increase the level of concern for an alternative's potential to cause adverse effects. IARC gives explicit guidance on the use of mechanistic data to support hazard assessments (for cancer).[100] The IARC Monograph preamble was developed with considerable international scientific comment and input, and has proven effective and scientifically defensible over the past decade of well over a hundred chemical reviews.

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[96] National Academies of Sciences, Engineering, and Medicine. 2015. Application of Modern Toxicology Approaches for Predicting Acute Toxicity for Chemical Defense. Washington, DC: The National Academies Press. doi:https://doi.org/10.17226/21775.

[97] National Academies of Sciences, Engineering, and Medicine. 2017. Using 21st Century Science to Improve Risk-Related Evaluations. Washington, DC: The National Academies Press. doi:https://doi.org/10.17226/24635

[98] Ibid.

[99] Cox LA, Popken D, Marty MS, Rowlands JC, Patlewicz G, Goyak KO, et al. Developing scientific confidence in HTS-derived prediction models: lessons learned from an endocrine case study. Regul Toxicol Pharmacol [Internet]. 2014 Aug [cited 2015 Oct 22];69(3):443–50.

Rotroff DM, Dix DJ, Houck KA, Knudsen TB, Martin MT, McLaurin KW, et al. Using in vitro high throughput screening assays to identify potential endocrine-disrupting chemicals. Environ Health Perspect [Internet]. 2013 Jan [cited 2015 Oct 1];121(1):7–14.

[100] International Agency for Research on Cancer. Preamble to the IARC Monographs: Mechanistic and Other Relevant Data [Internet]. Lyon, France; 2006 [cited 2015 Oct 26]. Available from: http://monographs.iarc.fr/ENG/Preamble/currentb4studiesother0706.php

2(k) Risk estimate approaches offer benefits over Margin of Exposure.

EPA requested comment about the strengths and weaknesses of the margin of exposure ("MOE") approach.[101] NRDC offers the following comments in response, and notes that our suggestions for risk estimate approaches would best be implemented by guidance or other policy documents.

EPA has traditionally used MOE analysis for evaluating chemical risks from non-cancer health effects. Its calculated MOEs played an important role in the Workplan risk assessments it conducted under the old law on trichloroethylene ("TCE") and other chemicals and are now part of the unreasonable risk determinations included in EPA's recent proposed rules for these chemicals under section 6(a) of TSCA. While these MOEs may be insufficiently conservative and protective, there is no doubt that they provide a strong basis for concluding that the uses targeted in the EPA rulemakings present serious and unacceptably great risks under well-established agency benchmarks. Indeed, the MOEs may understate the risks.

Moving forward, NRDC agrees with the NAS report, *Science and Decisions*, that EPA should avoid using MOE, Reference Dose ("RfD"), Reference Concentration ("RfC") or other similar approaches that are not quantifiable risk estimates in its risk evaluations for cancer or non-cancer risks.[102] Additionally, MOEs are more difficult for stakeholders to understand because it is counter-intuitive that a lower MOE is of greater concern than a higher MOE. This confusion is a barrier towards meaningful stakeholder engagement that should be avoided.

EPA should use the methodologies recommended by the NAS to harmonize assessment of cancer and non-cancer risk so that both can be evaluated using a risk-based approach to decision-making. EPA should generate quantitative risk estimates for both cancer and non-cancer endpoints, rather than the unprotective 'threshold' presumption that EPA now applies to non-carcinogens.

EPA's current approach to evaluating risks for any health effects other than cancer is to assume that there is a 'safe' exposure level below which negligible or no health effects will occur (a "threshold" of response). This is in contrast to the practice for carcinogens that assumes there is no threshold unless shown otherwise. Newer science is finding many examples of chemicals that increase the risk of various non-cancer health effects - such as reproductive harm and neurological effects - at low doses, without any scientifically-identifiable threshold.[103] *Science and Decisions* noted many differences in the

[101] 82 Fed. Reg. 7572

[102] "The end products of noncancer (and nonlinear cancer) assessments in the current paradigm (exposure-effect quotients that qualitatively indicate potential risk—MOEs, RfDs, and RfCs, Figure 5-1) are inadequate for benefit-cost analyses or for comparative risk analyses. MOEs and RfDs as currently defined do not provide a basis for formally quantifying the magnitude of harm at various exposure levels." National Research Council, 2009. Science and Decisions: Advancing Risk Assessment, Washington, D.C.: National Academies Press. pg. 133

[103] Grandjean P, Bellinger D, Bergman A, et al. 2008. The Faroes Statement: Human Health Effects Of Developmental Exposure To Chemicals In Our Environment. Basic Clin Pharmacol Toxicol. 102(2):73-5.

Grandjean P, Landrigan PJ. 2006. Developmental neurotoxicity of industrial chemicals. Lancet. 16;368(9553):2167-78.

Grandjean P, Landrigan PJ. Neurobehavioural effects of developmental toxicity. 701 Lancet Neurol. 2014, 13, (3),

population due to age, disease status, and nutrition. These factors plus the fact that people are exposed to multiple chemicals makes it very unlikely that a threshold exists across a diverse population, even if a threshold were to be established in an individual. This means that there may be no "safe" exposure across a diverse human population for many chemicals. For this reason, the *Science and Decisions* report recommends that a conceptual model be developed that is "from linear conceptual models unless data are sufficient to reject low-dose linearity; and nonlinear conceptual models otherwise."[104] EPA's practice should treat non-mutagenic carcinogens similarly to mutagenic carcinogens, presuming for both that there is no safe level of exposure (i.e. non-threshold toxicants with dose-response linearity). In addition, increased susceptibility of *in utero* and early life-stages and sensitive populations should be assumed for both mutagenic and non-mutagenic carcinogenic agents, as is done by California EPA[105] (see section 3(h) for more detail).

To yield the most useful information for decision-making, *Science and Decisions* recommends calculations of probabilistic risk distributions for cancer and non-cancer effects using a spectrum of evidence from humans, animals, mechanistic and other relevant studies.[106] These probabilistic risk distributions, incorporating variability of responses in the population (including sensitive subpopulations) and any existing uncertainty in the data available, should be used to quantify the risk associated with a particular level of exposure, including central tendency/ average and high-end exposures.[107] This will help to ensure that EPA's risk evaluations fully capture potential risks posed by exposure to unsafe chemicals. Further, such an approach will inform the process of risk-based decision making to ensure that risk management decisions are appropriate and based on complete information.

3. Strengths of EPA's proposal

Risk Evaluation Process

3(a) EPA appropriately proposes to not codify certain definitions to allow flexibility to stay current and adapt to the latest science.

In the Procedures for Prioritization of Chemicals for Risk Evaluation Under the Toxic Substances Control Act Proposed Rule[108] ("Proposed Prioritization Rule") and the Procedures for Chemical Risk Evaluation

330-338

[104] National Research Council, 2009. Science and Decisions: Advancing Risk Assessment, Washington, D.C.: National Academies Press. pg. 144

[105] Cal EPA 2009. California Environmental Protection Agency, Office of Environmental Health Hazard Assessment. Technical Support Document for Cancer Potency Factors: Methodologies for derivation, listing of available values, and adjustments to allow for early life stage exposures. http://oehha.ca.gov/media/downloads/crnr/tsdcancerpotency.pdf

[106] National Research Council, 2009. Science and Decisions: Advancing Risk Assessment, Washington, D.C.: National Academies Press pp.135-9

[107] Id. Ch. 5

[108] Procedures for Prioritization of Chemicals for Risk Evaluation Under the Toxic Substances Control Act; 82 Fed. Reg. 4825 (proposed January 17, 2017) (to be codified at 40 C.F.R 702)

Under the Amended Toxic Substances Control Act[109] ("Proposed Risk Evaluation Rule"), EPA requests comments on whether to include a definition or codification of scientific terms in the rules. Specifically, EPA seeks comments on defining terms such as "best available science," "weight-of-the-evidence," and "sufficiency of information" within the final rules.[110]

As EPA stated in the preamble of both rules: "Defining these and other scientific terms in the proposed rule is unnecessary and ultimately problematic. These terms have and will continue to evolve with changing scientific methods and innovation. Codifying specific definitions for these phrases may inhibit the flexibility of the Agency to quickly adapt and implement changing science."[111] Rather than codifying terms in the Final Rule, the Agency proposes to use "existing guidance definitions" and updates to the guidance documents as necessary. NRDC supports this approach as consistent with both the science and the construct of the law.

The legal context for this issue is instructive. First, none of these terms are defined in statute, including "weight of evidence" on which Congress requires EPA to base its Section 6 decisions pursuant to Section 26(i) of TSCA. The lack of definitions indicates Congressional reluctance to restrict the Agency's flexibility in applying these terms to Section 6 actions.

Second, under Section 26(l)(1) of TSCA, EPA is required to issue new "policies, procedures, and guidance" as needed to implement Section 6 (and other aspects) of TSCA. The language expressly refers to policies and guidance, thereby acknowledging the continuing role these administrative mechanisms would retain in the revised law. Moreover, the statutory deadline for discharging this obligation, June 22, 2018, is after the statutory deadline for completing the prioritization and risk evaluation rules, and thus strong evidence of Congressional intent that the rules will be augmented by policies and guidance as needed to implement Section 6 of TSCA.

Third, Section 26(l)(2) of TSCA further provides for mandatory, ongoing five year reviews of the "policies, procedures and guidance" developed under paragraph (1), and requires EPA to revise these materials and mechanisms as needed "to reflect new scientific developments or understandings." Congress expressly accounted for the evolving nature of science, and required EPA to update the science underlying the policies and guidance. Congress did not include a comparable five year review mandate for the prioritization and risk evaluation rules, thereby indicating the Congressional preference for using policies and guidance as needed in this context.

Lastly, we note Congress established a Science Advisory Committee on Chemicals ("SACC") under Section 26(o) of TSCA, charged with providing "independent advice and expert consultation" on the "scientific and technical aspects" of issues arising under TSCA. Therefore, when developing and reviewing the scientific policies and guidance under Section 26(l) of TSCA, interpreting weight of evidence under Section 26(i), and making technical decisions and policies regarding "reasonably available information" under Section 26(k) of TSCA, EPA can and should access the SACC for advice on the latest science underlying these matters, and need not restrict them through regulations.

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[109] Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act; 82 Fed. Reg. 7562 (proposed January 19, 2017) (to be codified at 40 C.F.R. pt. 702).

[110] As discussed below, since EPA did not propose any definitions of these terms, EPA cannot promulgate a final rule containing definitions of these terms without first proposing specific language for public comment.

[111] 82 Fed. Reg. 4828; 82 Fed. Reg. 7572.

The Technical Problems with Stakeholder Suggestions to Codify Specific Scientific Definitions and Processes

To ensure and maintain an efficient risk evaluation process, the Agency must not create a system in which terms of scientific importance are unnecessarily restricted and should allow them to evolve with shifts in scientific thinking and discovery. Indeed, the terms "best available science," "weight-of-the-evidence," and "sufficiency of information" can all be expected to change over time and context, with definitions most efficiently defined in guidance documents rather than in a rule. The 21st century has been an explosive time for scientific discovery, particularly in the fields of hazard and exposure assessment, creating an environment in which shifts in the definitions of each of the terms highlighted in the preamble to the Proposed Prioritization Rule and Proposed Risk Evaluation Rule can be reasonably anticipated. The rapid advances seen in computational, biological, and chemical approaches to risk assessment[112] supports the Agency position that the final prioritization and risk evaluation rules, should not "unduly [restrict] the specific science that will be used to conduct the evaluations."[113] To ultimately ensure the protection of human and environmental health in its TSCA evaluations in the future, the Agency must maintain the "flexibility to adapt and keep current with changing science."[114] We discuss some examples of the problems with codifying scientific terms and processes in greater detail below.

As we discuss more conceptually above, the desire from some stakeholder groups for explicit definitions of terms within the final rules[115] has the potential to substantially decrease the flexibility of the Agency to respond to change in the scientific landscape and thereby impede EPA's TSCA implementation. We address some specific examples here. For instance, the American Chemistry Council has recommended that EPA define the terms "best available science" (and other similar terms), "weight of evidence" ("WOE"), and "sufficiency of information," as well as explicitly define processes or mechanisms by which to evaluate hazard, exposure, or dose response assessments. Each of these suggestions raises concerns.

The term "best available science," while often used, is an amorphous, judgement-laden concept that can shift over time. For example, the use of mechanistic information has changed significantly within EPA cancer assessments. While the 1986 USEPA Guidelines for Carcinogen Risk Assessment[116] utilizes mechanistic information in a more limited way – going so far as to state that "[a]t present, mechanisms of the carcinogenesis process are largely unknown and data are generally limited," mechanistic data became an important source of information in the 2005 Guidelines for Carcinogen Risk Assessment.[117] Had "best available science" been defined solely as the use of whole animal systems or epidemiologic studies, an important evidence stream could be missing from or unusable in current cancer

[112] National Academies of Sciences, Engineering, and Medicine. 2017. Using 21st Century Science to Improve Risk-Related Evaluations. Washington, DC: The National Academies Press. doi:https://doi.org/10.17226/24635

[113] See pg. 7567; Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act; 82 Fed. Reg. 7562 (proposed January 19, 2017) (to be codified at 40 C.F.R. pt. 702).

[114] Ibid.

[115] For example, see "ACC Comments to Inform EPA's Rulemaking on the Conduct of Risk Evaluations under the Lautenberg Chemical Safety Act", in EPA docket "Meetings: Processes for Risk Evaluation and Chemical Prioritization for Risk Evaluation under the Amended Toxic Substances Control Act", comment ID: EPA-HQ-OPPT-2016-0400-0028.

[116] U.S. EPA. Guidelines for Carcinogen Risk Assessment (1986). U.S. Environmental Protection Agency, Washington, DC, EPA/630/R-00/004, 1986.

[117] U.S. EPA. Guidelines for Carcinogen Risk Assessment (2005). U.S. Environmental Protection Agency, Washington, DC, EPA/630/P-03/001F, 2005.

assessments.

Congress itself found defining the term "best available science" to be a difficult proposition. The original legislation that was the starting point for what was eventually enacted into law included a definition of the term. That provision was abandoned in later versions of the legislation and was not included in the final law.[118] This decision was in keeping with a more general trend from the first introduced version of the legislation to the final enacted version of removing most of the heavily prescriptive science-policy language, and ultimately providing the EPA with some general direction and a great deal of discretion, as is reflected in Section 26(h) of the final law.[119]

Similarly, the term "sufficiency of information" should not be defined within the final Prioritization or Risk Evaluation rules. "Sufficiency of information" is an ill-defined concept that has no clear scientific definition, nor is its use mandated by the statute. Information needs can vary significantly based upon the stage of an evaluation (e.g., prioritization versus risk assessment versus risk management), and an inflexible definition could limit the consideration of the appropriate science. For instance, as discussed in a recent report released by the NAS,[120] tools like chemical read-across (i.e., using data from well-studied, existing chemicals to predict the toxicity of chemicals with limited data based upon similar structure, biological activity, or metabolism) could be appropriately used for some purposes, but that "[r]ead-across can be problematic, and caution is needed before its conclusions are relied on heavily."[121] Read-across methods could be sufficient for upgrading the designation of a chemical (e.g., identifying a chemical as "high priority") or for chemical screening, such as narrowing the chemicals to undergo Tier 1 and Tier 2 screening in the Endocrine Disruptor Screening Program, but would not be sufficient as the sole source of information to downgrade a chemical classification (e.g., identifying a chemical as "low priority").

Defining the concept of "weight of evidence" also raises concerns. The definition of WOE is triply troubling: it varies with context, it is vague, and there are numerous definitions in use. The NAS report, *Science and Decisions* describes WOE as a phrase used to "describe the strength of the scientific inferences that can be drawn from a given body of evidence."[122] It noted that WOE evaluations "[vary] greatly among chemicals and other hazardous agents in type, quantity, and quality."

The NAS consequently concluded that "it is not possible to describe the WOE evaluation in other than relatively general terms. It is thus not unexpected that WOE judgements in particular cases can vary among experts and that consensus is sometimes difficult to achieve."[123] Similarly, the National Research Council 2014 report on the Review of EPA's IRIS Process found that the phrase WOE had become "far too vague as used in practice and thus is of little scientific use."[124]

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[118] See Chemical Safety Improvement Act of 2013, S.1009, page 7, lines 14-23.

[119] Compare for example CSIA, p. 14, line 1 -- p. 15, line 4 to the final Section 26(h).

[120] National Academies of Sciences, Engineering, and Medicine. 2017. Using 21st Century Science to Improve Risk-Related Evaluations. Washington, DC: The National Academies Press. doi:https://doi.org/10.17226/24635.

[121] Ibid at pg 78.

[122] National Research Council, 2009. Science and Decisions: Advancing Risk Assessment, Washington, D.C.: National Academies Press. pg 88.

[123] Ibid.

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

The 2014 committee also found various definitions in existence, including seemingly simplistic balancing equations with evidence supporting hazard on one side and evidence refuting hazard on the other to more intricate "systematic review" processes with pre-established protocols and comprehensive inclusion of a variety of data sources. These definitions each proved unsatisfactory to the committee, with the committee ultimately recommending abandoning "weight of evidence" and instead employing the term "evidence integration" as a more appropriate and useful term for the data integration step involved in IRIS assessments.

In addition to the dangers of defining scientific terms, explicitly defining processes or mechanisms by which to evaluate hazard, exposure, or dose response assessments is overly restrictive.[125] While the overarching framework for risk assessment in federal regulatory decisions has remained largely unchanged since the 1983 publication of Risk Assessment in the Federal Government: Managing the Process[126] or "the Red Book," the tools used to generate information and the processes by which to interpret those data is an ever changing and ongoing process. As highlighted extensively in the recent National Academies of Sciences report, "Using 21st Century Science to Improve Risk-Related Evaluations,"[127] the increased use of probabilistic statistical methods and computational tools, not yet discovered or used in wide practice when the Red Book was printed have the potential to significantly alter the ways in which modern risk assessment is and will be conducted.

As these examples demonstrate, the codification of a WOE within a rule that requires a lengthy legal process before changes can be made can severely limit the ability of the Agency to use the most appropriate tools to evaluate the potential risks posed by chemicals in products and the environment.

While the definition of these scientific terms should not be fixed in the final Prioritization or Risk Evaluation rules, NRDC strongly supports transparency in the WOE narratives and determinations associated with the processes these terms reference. It is essential to public trust that the inclusion and exclusion criteria for specific studies and lines of evidence be presented in a transparent and accessible way.

Systematic review

EPA is requesting comment on the need for regulatory text regarding specific elements of systematic review. NRDC believes that a detailed systematic review method should not be codified, for the same reasons described above: generally to be able to integrate ongoing methods development as advances take place. This is, for example, the approach of the NTP, that enables the agency to stay actively engaged with the academic community and practitioners of systematic review, to ensure that its methods remains flexible and can be continuously updated to reflect the state-of-the-science.[128]

[125] See, for example, pages 15-17 and appendices B, C, and D of "ACC Comments to Inform EPA‟s Rulemaking on the Conduct of Risk Evaluations under the Lautenberg Chemical Safety Act", in EPA docket "Meetings: Processes for Risk Evaluation and Chemical Prioritization for Risk Evaluation under the Amended Toxic Substances Control Act", comment ID: EPA-HQ-OPPT-2016-0400-0028

[126] National Research Council. 1983. Risk Assessment in the Federal Government: Managing the Process. Washington, DC: The National Academies Press. doi:https://doi.org/10.17226/366.

[127] National Academies of Sciences, Engineering, and Medicine. 2017. Using 21st Century Science to Improve Risk-Related Evaluations. Washington, DC: The National Academies Press. doi:https://doi.org/10.17226/24635

[128] NTP Systematic Review ongoing methods development activities

3(b) NRDC supports EPA's approach to 'reasonably available' information in the framework of the prioritization and risk evaluation proposals.

As the emphasis on intended, known, or reasonably foreseeable uses indicates (see discussion above in "Conditions of Use" section), in both prioritization and risk evaluation, the availability of information for chemical assessments is critical for the timely completion of each task. In the proposed rule on risk evaluation, the Agency has defined "reasonably available" information as "existing information that EPA possesses, or can reasonable obtain and synthesize for use in risk evaluations, considering the deadlines for completing the evaluation."[129] This definition of "reasonably available" is appropriate within the front-loaded prioritization and risk evaluation framework proposed by EPA and by extension to the prioritization process.

This front-loaded process requires that EPA compile available information before prioritization to ensure an efficient prioritization and risk evaluation process, particularly to identify and fill data gaps under its data collection authority, including those under TSCA sections 4, 8, and 11(c). As EPA has stated, "EPA generally expects to pursue a significant amount of data gathering before initiating prioritization."[130]In this context, EPA's proposal for information accumulation in this proposed rule should be improved. EPA has proposed a rule which states that if, after the screening review, EPA does not "believe" that it has sufficient information for a priority designation, it is "likely" to use its information gathering authorities to generate the necessary information before pursuing prioritization. Instead of leaving things so open-ended, we recommend that EPA reflect the preamble intent in the regulatory language by replacing the relevant language with the phrase "EPA shall use its information gathering authorities under the Act as needed to meet the Agency's risk evaluation obligations under the Act."

To guarantee that ample information is collected and data gaps are appropriately identified, the Agency should develop a process for identifying the information necessary for completing a risk evaluation in the pre-prioritization phase of chemical assessments. Potential sources of information should be outlined for each condition of use for each chemical or class of chemicals related to, but not limited to: chemical properties (e.g., physical and chemical characteristics, related chemistries, metabolic potential, etc.), sources of hazard and dose response information (e.g., animal, non-animal, epidemiologic, mechanistic studies, etc.), sources of aggregate and cumulative exposure information (e.g., sources of near- and far-field exposure including environmental release information, production volume, presence in consumer and household products, dietary intake, occupational exposure, modeling tools with mechanisms for quantifying uncertainty and variability, etc.), and sensitive and/or vulnerable subpopulations.

When outlining the information necessary for the successful completion of the prioritization, scoping, and risk evaluation steps of a chemical assessment, the Agency has several internal processes that could be employed. For example, for hazard assessment, the Safer Choice Master Criteria for Safer Chemical Ingredients provides a useful matrix for organizing and collecting information across multiple attributes of concern (e.g., acute mammalian toxicity, carcinogenicity, genetic toxicity, etc.) for chemicals and

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https://ntp.niehs.nih.gov/pubhealth/hat/noms/index-2.html#Ongoing-Methods-Development-Activities

[129] 82 Fed. Reg. 7568

[130] 82 Fed. Reg. 4828, col. 3 (January 17, 2017).

chemical classes[131].

In addition to the Safer Choice Master Criteria, another resource that the Agency could utilize and build upon for organizing exposure-based information is the Draft Exposure Guidelines.[132] Though the document is still in draft form, it provides an organizational frame for gathering information necessary to complete a comprehensive exposure assessment.

Once essential information and sources have been identified, the Agency should also seek to organize initial findings in a way that is easily accessible and transparent. For example, the existing framework for generating scoping documents during the pesticide registration review process provides a systematic method for walking through data sources and data gaps. These scoping documents provide clearly delineated sections for information collected across risk assessment domains (e.g., hazard and exposure), sources of information, highlight gaps in knowledge, and give rationale for particular decision points.

The examples listed above are not meant to be inclusive, and are not intended to suggest procedures that should be codified within the final rule, but instead seek to illustrate ways in which the Agency can facilitate efficient data gathering exercises and help identify specific mechanisms to acquire missing/needed information in the pre-prioritization, prioritization, scoping, and risk evaluation processes via internal processes and guidance documents as appropriate.

As a structural device for organizing and managing the flow of information to the Agency, we recommend the development of a chemical-specific roadmap during the screening stage of the process. The roadmap would start with identifying the types and categories of information the Agency needs to complete the scoping document for the chemical, as discussed above and as proposed in the risk evaluation notice at 40 CFR 702.39(c).[133] The roadmap would then indicate the information EPA possesses at the time, the data gaps remaining, the tools EPA has or intends to utilize to obtain the needed data, and the timetable for receipt of the information. EPA would make the roadmap available for public review and comment no later than when it publishes the Federal Register notice initiating the prioritization process for the chemical.[134] Ideally, EPA would be reaching out to stakeholders during the screening process to solicit information on conditions of use, hazards, exposures, and use of information gathering authorities, including a working draft roadmap.

3(c) EPA's proposal on manufacturer requested risk evaluations is appropriate.

NRDC supports the approach to considering and processing manufacturer requested risk evaluations as described in the Agency's Proposed Rule. In particular, NRDC supports the Agency's requirement that the requesting manufacturer(s) provide EPA (and the public) with the information necessary to evaluate the risks posed by the chemical for all conditions of use, throughout the entire lifecycle of the substance,

[131] U.S. Environmental Protection Agency. Safer Choice Master Criteria for Safer Chemical Ingredients Available at: https://www.epa.gov/saferchoice/safer-choice-master-criteria-safer-chemical-ingredients. Accessed 2/24/2017

[132] USEPA 2016. Guidelines for Human Exposure Assessment. Risk Assessment Forum, Peer Review Draft.

[133] 82 Fed. Reg. 7577 (January 19, 2017).

[134] The Agency should be well positioned to specify the information gaps and tools it will use to fill the gaps by the time the prioritization process is initiated, since under proposed 40 CFR 702.7(f), EPA is "likely" to use its TSCA authorities to fill data gaps before initiating prioritization. See 82 Fed. Reg. 4836 (January 17, 2017).

as is required for chemicals being evaluated through the regular process established under the newly revised law. As noted elsewhere in these comments, we also support EPA's proposed requirement that companies provide upfront substantiation and certification for any non-exempt claims of CBI.

EPA's approach to ensuring that the Agency has all the information necessary to conduct a manufacturer-requested risk evaluation prior to initiating such an evaluation under the statutory deadlines is reasonable. As noted elsewhere in our comments, the revised TSCA requires EPA to consider all conditions of use for a chemical, including those known, intended, and reasonably foreseeable, for the entire lifecycle of the chemical, and the law requires EPA to obtain the information necessary to make a determination about whether the uses of the chemical pose an unreasonable risk.

The law lays out a process and provides EPA with the tools to obtain the necessary information, including its information gathering authorities under sections 4, 8 and 11. Where the law provides chemical manufacturers with a separate process for self-nominating its chemicals for evaluation, it makes sense that those companies should need to meet the same requirements for data and information on hazard, exposure and uses, and that the burden of producing those materials is on the manufacturer(s). The law makes no distinctions regarding the standard for and the requirements of the risk evaluation determinations based upon who initiates the process.

The approach proposed by EPA facilitates evaluation of a chemical for which there is a single manufacturer, or for which there is consensus amongst the manufacturers regarding the desirability of EPA conducting an evaluation of the substance. Given the law's mandate to consider all conditions of use of a chemical, throughout the lifecycle of the substance, and the consequent need for an extensive amount of information to conduct a proper evaluation, this approach makes sense. In the absence of such an approach, EPA would instead be compelled to use its existing authorities under Sections 4, 8 and 11 of the Act to obtain information from companies that are not interested in volunteering or requesting that their chemical be subject to a risk evaluation, and thus inappropriately moves the process toward the EPA initiated screening process. Under the approach proposed by EPA, the Agency need not be in the awkward position of negotiating between those manufacturers of a chemical who seek to use the industry-request option for having a chemical evaluated and those who don't.

NRDC also supports EPA's proposal to give preference to those substances for which there are "relatively high estimates for hazard and/or exposure"[135] in determining which chemicals warrant risk evaluations. The purpose of TSCA is to evaluate the safety of chemicals and protect the public from those that are unsafe. The history of the law's prolonged lack of effectiveness is well known, resulting in an enormous backlog of chemicals -- including hundreds with troubling hazard and exposure profiles – for which EPA must now conduct risk evaluations and, where necessary impose restrictions. The Agency now faces a host of mandatory deadlines and minimum requirements to address the backlog, at a time of limited and potentially declining resources. Congress clearly signaled its desire for EPA to focus on the "worst first," as illustrated by the emphasis on Work Plan chemicals, PBTs and identifying "high priority" chemicals for risk evaluation. It is only rational for the Agency to focus on those chemicals for which available evidence suggests the greatest potential risk, and presumably that was the point of fashioning the prioritization process the way Congress did, to direct EPA's limited resources toward evaluating those chemicals deemed to be the highest priority. EPA's approach to similarly prioritizing the chemicals presented to the Agency for review under the Industry-request provision of the statute is

[135] proposed Sec. 702.37 (e)(5)(ii)

both consistent with and rational within the statutory scheme developed by Congress.

As noted above, NRDC supports EPA's proposal to include an opportunity for public comment and input on information regarding uses of the chemical, as well as information on hazard and exposure.[136] However, 30 days is an insufficient amount of time to analyze the information EPA will have already collected and develop thorough substantive comments to assist the Agency. We note that where EPA initiates the prioritization process, the public will have the opportunity to comment at both the screening and scoping phases to identify conditions of use and exposure scenarios of concern. However, under the manufacturer-initiated process, these two phases are essentially compressed into one, and thus the comment period here needs to be longer to account for the reduced number of comment opportunities. NRDC recommends that the final rule provide for a 90 day period for public notice and comment.

Finally, NRDC supports EPA's proposal to reject nomination petitions for which the information provided by industry is inadequate to properly evaluate the substance. EPA is proposing a minimum number of reasonable requirements to allow the Agency to conduct risk evaluations that will meet the standards established by Congress under the revised law. If companies cannot or will not produce the information needed, or take the other necessary steps (like substantiation and certification of CBI claims), it would be improper for the Agency to move forward and initiate the risk evaluation. Notably, EPA explicitly preserves the right of a company to submit a request for risk evaluation for the same chemical at a later date, so there is no prejudice to the manufacturer(s) if its first attempt is inadequate or is withdrawn.

3(d) EPA is not required to implement animal testing or Section 26 provisions by rule.

EPA notes that it is not proposing to address a number of statutory requirements as part of the risk evaluation rule, including those pertaining to the issue of animal testing in Section 4(h) [15 U.S.C. 2603(h)] and the science policy provisions of Section 26(h) and (i) [15 U.S.C. 2625 (h) and (i)].[137] NRDC supports this approach and EPA should not change its approach in the final rule.

As EPA notes in the preamble, the statute does not require either the animal testing provisions or the Section 26 provisions to be implemented by rule. Nor would it make sense for EPA to do so, since they address policies that are evolving and will continue to evolve, and are not provisions that lend themselves to being locked into a single codified approach through rulemaking. For example, the bulk of the "animal-testing" provisions of section 4(h) pertains to a Strategic Plan to reduce testing on vertebrate animals, the first version of which is not even due to be produced by EPA under the statute until June 2018 and for which EPA must submit updates and goals for future implementation strategies to Congress every five years. It simply makes no sense to lock the Agency into a particular approach via rulemaking for a plan of action that has yet to even be developed, and which will itself be forward-looking and presumably develop in response to new science and understanding over time. Congress encouraged efforts to reduce the amount of testing on vertebrate animals as an ongoing and evolving process that EPA would implement in parallel with its ongoing obligations for prioritization, risk evaluation and risk management, without it being wholly intertwined or binding EPA to a particular

[136] See 82 Fed. Reg. 7569 (col.3) and proposed Sec. 702.37, at 7577 (col.2)
[137] 82 Fed. Reg. 7565

method or approach at the outset.

Similarly, the "science policy" provisions of Sections 26(h) and (i) are not appropriate for codification via rulemaking as part of the risk evaluation process. As noted in our discussion regarding codifying definitions elsewhere in these comments, certain terms and concepts – because they are central to science policy discussions – are not easily defined, and do not lend themselves to freezing into a particular meaning as part of a rulemaking.

The legislative history of the science policy provisions of Sections 26 (h) and (i) underscore the desire of Congress *not* to narrowly constrain the Agency's flexibility to interpret and apply the requirements. The earlier versions of the science policy provisions that ended up in Section 26(h) and (i) are greatly reduced in number, and are both less defined and less prescriptive than those that existed in the earliest versions of the legislation, starting with the original version of the Chemical Safety Improvement Act in May 2013. [138]

In sum, EPA has discretion under the law whether or not to implement these provisions via rulemaking, and it is right not to do so. In addition, if EPA were to change course and decide to codify either the animal testing or science policy provisions, the Agency would need to re-propose the risk evaluation rule for another round of notice and comment, something that cannot be done and still meet the statutory deadlines for issuance of the final risk evaluations rules.

Risk Evaluation Components

3(e) EPA appropriately excludes the vague term "fit for purpose" from the rule; EPA must reference the data and assumptions underlying conclusions for all analyses that are part of a risk evaluation.

The phrase "fit for purpose" does not appear in the revised TSCA. Section 6(b)(4)(F), listing the requirements for a risk evaluation. EPA has appropriately not included the phrase "fit for purpose" in its risk evaluation proposal, though the Agency does describe one interpretation of the phrase and its potential application: "All conditions of use will not warrant the same level of evaluation, and EPA expects it may be able to reach conclusions without extensive or quantitative evaluations of risk."[139]

NRDC agrees this may be the case; however in order to meet the statutory requirement to determine unreasonable risk to a potentially exposed or susceptible population, EPA must ensure that all components of the risk evaluation, for all uses, are robust enough to determine contribution to the real-world aggregate exposure experienced by the most vulnerable population. For the example described in the preamble/background, of a "lower volume" or "less-dispersive use,"[140] EPA would need to clearly document the data and assumptions used to draw conclusions about potential risks resulting from those

[138] For example, compare Chemical Safety Improvement Act of 2013, S.1009, p. 14, line 1 -- p.15, line 4 to the final Section 26(h).
[139] 82 Fed. Reg. 7566
[140] Id.

uses, regardless of the level or complexity of the analysis. In previous assessments of flame retardant chemicals, the Agency presented conclusions about the 'likelihood of low risk concerns' from drinking water exposures without documentation of the data, sources, or evidence used to reach this conclusion.[141]

When the Agency conducts a risk evaluation, an exposure cannot be excluded from the aggregate exposure analysis (now mandated by law as discussed above) solely because it individually seems to be "low risk;" exposures add up, and many small exposures may add up to an exposure of concern. All available quantitative exposure data should feed into the aggregate exposure analysis, even if different levels of evaluation/ analysis were used in the calculations for some conditions of use or exposure pathways.

Finally, EPA's *Framework for Human Health Risk Assessment to Inform Decision Making* describes an interpretation of the "fit for purpose" approach that involves targeting risk evaluation toward risk management options.[142] This approach would be inconsistent with TSCA, which requires the Agency to comprehensively evaluate conditions of use and aggregate exposures to susceptible populations, regardless of what risk management options may or may not be available. Congress expressly excluded such non-risk factors from consideration in reaching unreasonable risk determinations.

3(f) NRDC supports EPA's approach to identify potentially exposed or susceptible subpopulations.

The new law appropriately focuses on protecting the most vulnerable- in the terms used by the statute, "potentially exposed or susceptible subpopulations." In its discussion of definitions, EPA proposes to "expand" the definition of "potentially exposed or susceptible populations" by proposing to insert the clause "including but not limited to" before the specific subpopulations that are enumerated in the statutory definition of the term.[143] EPA says that this is intended "to further clarify that EPA may identify additional subpopulations, where warranted."[144] While NRDC concurs with EPA's proposed regulatory definition, EPA's characterization of this clause as a needed clarification of its authority to identify additional subpopulations at risk is incorrect. The statutory language itself can only be read to mean that the enumerated subpopulations are examples, not the total set of potential subpopulations: "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population *identified by the Administrator* who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, *such as* infants, children, pregnant women, workers, or the elderly."[145]

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[141] US EPA, August 2015. TSCA Work Plan Chemical Problem Formulation and Initial Assessment: Tetrabromobisphenol A and Related Chemicals Cluster Flame Retardants.

[142] According to the Framework: "The overarching questions in addressing 'fit for purpose' are the following: Does the assessment inform choices among risk management options? Will the risk assessment need to be changed or expanded to discriminate between risk management options?" Office of the Science Advisor, EPA, Framework for Human Health Risk Assessment to Inform Decisionmaking at 4 (2014), available at https://www.epa.gov/sites/production/files/2014-12/documents/hhra-framework-final-2014.pdf

[143] 82 Fed. Reg. 7568

[144] Id.

[145] 15 U.S.C. 2602 (12)(emphases added)

Two separate clauses of the statutory definition make clear that Congress did not intend to limit the scope of whom or what might be considered a "potentially exposed or susceptible subpopulation" under the law. The definition explicitly gives the EPA the authority to identify those vulnerable populations to be considered under the law, making clear that it was not a determination to be made, or limited, by Congress. Moreover, the use of the clause "such as" before the list of specific subpopulations in the definition makes crystal clear that the list that follows the clause is not intended to be exclusive. Indeed, "including but not limited to" is essentially synonymous with the "such as" used by Congress in its statutory definition. Accordingly, the clause "including but not limited to" is properly viewed as a restatement of the statutory definition, and nothing more.

While EPA states that protecting vulnerable populations is not a new consideration for the Agency,[146] its past actions in this area, especially concerning environmental justice and fence-line communities, have fallen far short. A recent report from the U.S. Commission on Civil Rights noted:

> "The Commission's review of EPA's compliance with its environmental justice obligations revealed two major reoccurring themes. First, EPA continues to struggle to provide procedural and substantive relief to communities of color impacted by pollution. EPA's deficiencies have resulted in a lack of substantive results that would improve the lives of people living in already overly-burdened communities. Second, EPA does not take action when faced with environmental justice concerns until forced to do so. When they do act, they make easy choices and outsource any environmental justice responsibilities onto others."[147]

The Commission's sobering evaluation highlights the ongoing need for, and importance of, protecting environmental justice communities and other vulnerable populations, as recognized by Executive Order 12898[148] on environmental justice.

Accordingly, NRDC agrees with EPA's proposal to consider intrinsic and 'acquired' characteristics to identify potentially exposed or susceptible subpopulations. Intrinsic characteristics include biological traits such as age and life stage. Acquired characteristics include factors like socioeconomic status and geography. It is critical that EPA consider both types because a significant body of science supports that intrinsic and acquired characteristics can contribute to increased susceptibility, as noted by *Science and Decisions*:

"Individuals may be more vulnerable than others because they have or are exposed to

- Factors that increase biologic sensitivity or reduce resilience to exposures (such as age, pre-existing disease, and genetics).
- Prior or concurrent exposures to substances that increase a person's susceptibility to the effects of additional exposures.

[146] 82 Fed. Reg. 7565

[147] U.S. Commission on Civil Rights.(2016) Environmental Justice: Examining the Environmental Protection Agency's Compliance and Enforcement of Title VI and Executive Order 12,898. Available: http://www.usccr.gov/pubs/Statutory_Enforcement_Report2016.pdf

[148] Executive Order 12898 - Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations. 59 FR 7629; February 16, 1994

- Factors that contribute to greater potential for exposure, including personal behavior patterns, the built environment, and modified environmental conditions in locations where time is spent (such as community, home, work, and school).
- Social and economic factors that may influence exposure and biologic responses."[149]

State agencies and EPA have provided further description of relevant characteristics to consider. OEHHA considers biological traits (intrinsic factors) and community characteristics (acquired factors) that result in increased vulnerability to toxic effects in the California Communities Environmental Health Screening Tool, stating:

> "A growing body of literature provides evidence of the heightened vulnerability of people of color and lower socioeconomic status to environmental pollutants. For example, a study found that individuals with less than a high school education who were exposed to particulate pollution had a greater risk of mortality. Here, socioeconomic factors that have been associated with increased population vulnerability were selected."[150]

Biological (intrinsic) traits considered by OEHHA include impaired physiological conditions like heart disease and asthma; acquired factors considered include poverty, unemployment and educational attainment. The factors influencing susceptibility in EPA's EJScreen Technical Documentation are consistent with the intrinsic and acquired characteristics considered by OEHHA:

> "EPA places particular emphasis on the public health of and environmental conditions affecting minority, low-income, and indigenous populations...EPA should pay particular attention to the vulnerabilities of these populations because they have historically been exposed to a combination of physical, chemical, biological, social, and cultural factors that have imposed greater environmental burdens on them than those imposed on the general population...The demographic indicators in EJSCREEN are a way to indicate which communities may be more susceptible to a given level of exposure to environmental pollutants. For example, individuals may be more susceptible when they are already in poor health, have reduced access to care, lack resources or language skills or education that would help them avoid exposures or obtain treatment, or are at susceptible life stages."[151]

EPA's Draft Exposure Guidelines[152] reviews evidence for increased vulnerability based on all the intrinsic and acquired factors discussed above, plus others.

The science presented in the above sources indicates that EPA must consider a number of critical intrinsic and acquired factors in order to accurately identify potentially exposed or susceptible

[149] National Research Council, 2009. *Science and Decisions: Advancing Risk Assessment*, Washington, D.C.: National Academies Press. Pg. 110

[150] CA OEHHA, Jan 2017. Update to the California Communities Environmental Health Screening Tool: CalEnviroScreen 3.0. Available: https://oehha.ca.gov/media/downloads/calenviroscreen/report/ces3report.pdf

[151] US EPA, June 2016. EJSCREEN Environmental Justice Mapping and Screening Tool: Technical Documentation. Available: https://www.epa.gov/sites/production/files/2016-07/documents/ejscreen_technical_document_20160704_draft.pdf

[152] USEPA 2016. Guidelines for Human Exposure Assessment. Risk Assessment Forum, Peer Review Draft. Ch 4. pg. 39-60

subpopulations. These factors broadly include cumulative exposures, as well as chemical and non-chemical stressors.

3(g) NRDC agrees with EPA's proposal on categories of chemical substances.

NRDC supports EPA's proposal to make clear that any reference to chemical substances in the regulations encompasses categories of chemical substances as defined in the statute, including groups of chemical substances or mixtures which share similar properties. As EPA notes, the statute explicitly states that "[a]ny action authorized or required to be taken by the Administrator under any provision of this chapter with respect to a chemical substance or mixture may be taken by the Administrator in accordance with that provision with respect to a category of chemical substances or mixtures."[153]

3(h) Defaults and uncertainty factors are critical components of a risk evaluation.

EPA states that it will use accepted science policies, including defaults and uncertainty factors, in risk evaluations. NRDC agrees that appropriate defaults and uncertainty factors are critical components of a risk evaluation. NRDC offers the following general commentary on the implementation of appropriate defaults and uncertainty factors in risk evaluations.

Through guidance or other policy documents, EPA should make clear that health-protective assumptions are the default assumption in all cases and under all conditions; EPA should provide clear criteria for departing from defaults particularly where they lead to weakened health protections. When replacing a default with an alternative assumption for a particular chemical, EPA's risk evaluations should provide an explanation and quantify how using a default versus the chosen alternative assumption affects the decisions that protect the environment and public health.[154] Establishing, "clear criteria for departure from defaults can provide incentives for third parties to produce research" that can reduce uncertainty and, over time, result in more accurate assessments. Importantly, by using the established defaults more often, EPA's risk evaluations could avoid "the delay entailed by having to re-examine generic information with every new risk assessment."[155]

Science and Decisions recommends that EPA and other agencies update default factors and assumptions based on the best current science, identify where unstated or implicit assumptions are used, and replace these with explicit assumptions. These recommendations push EPA to, "continue and expand use of the best, most current science to support or revise its default assumptions,"[156] which make the assumptions stronger, rather than reducing reliance on them. At a minimum, EPA should use California EPA's age adjustment values and intraspecies uncertainty factors for incorporating age/early life susceptibility, as discussed below.

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[153] 15 U.S.C. § 2625(c).

[154] Janssen S, Sass J, Schettler T, Solomon G. 2012. Strengthening toxic chemical risk assessments to protect human health. NRDC Issue Paper. https://www.nrdc.org/sites/default/files/strengthening-toxic-chemical-risk-assessments-report.pdf

[155] National Research Council, 2009. Science and Decisions: Advancing Risk Assessment, Washington, D.C.: National Academies Press. p. 191

[156] Id. p. 207

Risk assessors with OEHHA reviewed the literature on differential susceptibility to carcinogens and non-carcinogens based on age and life stage. As a result of this review, OEHHA derived age adjustment values for carcinogens which include the prenatal period, determined that increased susceptibility of *in utero* and early life stages should be evaluated for both mutagenic and non-mutagenic carcinogenic agents,[157] and increased the default intraspecies uncertainty factors for non-carcinogens to 30 and 100 for specific endpoints such as asthma or neurotoxicity.[158]

In *Science and Decisions*, the committee noted that for cancer assessments differences in median versus higher-end response to carcinogens differ by a factor of 25.[159] It would be appropriate for EPA to quantitatively address this level of variability by multiplying all cancer risk estimates by a factor of 25 in its risk evaluations for an early-tier assessment of most cancer-causing chemicals, unless a greater level of detail is needed. Where data are available on population variability in susceptibility, EPA can support the use of larger uncertainty factors or increase the strength of epidemiologic or other evidence of harm.

As discussed in the section above on potentially exposed or susceptible subpopulations, multiple sources of contaminants; multiple contaminants that together pose a larger health threat because they act through a common pathway or impact similar health endpoints; and the combined impact of contaminant exposure with social stressors[160] all are documented to contribute to increased susceptibility. EPA should use default factors to account for the known additional risk coming from these sources where they cannot be more explicitly quantified.

While NRDC agrees with EPA that risk evaluations or risk characterizations may be quantitative or qualitative, quantitative approaches should be utilized and prioritized when the necessary information is reasonably available for the target subpopulations of concern. This is consistent with EPA's statutory obligation to assess aggregate risks, when relevant, as discussed earlier. However, in the absence of quantitative information, EPA should proceed with a qualitative evaluation rather than ignoring potential risks.

3(i) Hazard assessment.

The proposed rule appropriately indicates that the identification of human and environmental hazard endpoints (702.39(d)(2)-(3)) and the dose-response evaluation (702.39(d)(4)) are separate and discrete steps. As described in the proposed rule, hazard identification occurs first, followed by a dose-response

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[157] Cal EPA 2009. California Environmental Protection Agency, Office of Environmental Health Hazard Assessment. Technical Support Document for Cancer Potency Factors: Methodologies for derivation, listing of available values, and adjustments to allow for early life stage exposures.
http://oehha.ca.gov/media/downloads/crnr/tsdcancerpotency.pdf

[158] Cal EPA 2008. California Environmental Protection Agency, Office of Environmental Health Hazard Assessment. Technical Support Document For the Derivation of Noncancer Reference Exposure Levels
http://oehha.ca.gov/media/downloads/crnr/noncancertsdfinal.pdf

[159] National Research Council, 2009. *Science and Decisions: Advancing Risk Assessment*, Washington, D.C.: National Academies Press.

[160] Stein, L.J. et al., 2016. Early childhood adversity potentiates the adverse association between prenatal organophosphate pesticide exposure and child IQ: The CHAMACOS cohort. Neurotoxicology, 56, pp.180–187. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27474229

evaluation for one or more identified endpoints. EPA's Draft Exposure Guidelines similarly describe the four separate steps of risk assessment: Hazard identification, dose response assessment, exposure assessment and risk characterization.[161]

In identifying hazard endpoints, EPA may find the comprehensive description of hazard traits developed by Cal/EPA under California's Green Chemistry Initiative useful.[162]

The dose-response evaluation must consider non-monotonic dose response, especially for endocrine disrupting chemicals.[163] Zoeller, et al discusses the process of considering non-monotonic dose response in a risk assessment context.[164]

3(i)(i) Epidemiology and animal studies provide critical data for hazard assessment.

The proposed rule specifically states that EPA will include human epidemiological studies and *in vivo* laboratory studies along with other available data in its hazard assessments.[165] NRDC strongly supports the use of human epidemiologic studies and experimental animal studies, and offers the following general comments about these types of studies and their use in risk evaluation.

Data from toxicological studies in whole animals, usually rodents, are highly relevant for predicting toxicity in humans. For example, every agent that is known to cause cancer in humans is carcinogenic in animals when adequately tested;[166] and almost one-third of human carcinogens were identified after carcinogenic effects were found in well-conducted animal studies.[167] The reasons for this high level of concordance across species are several-fold: First, animals and humans are highly similar in many relevant conserved genetic, metabolic, and systemic processes that affect the biological processes of disease induction and progression. It is for this reason that animal tests, conducted in accordance with strict guidelines for the welfare and use of research animals, are required by regulatory bodies before new pharmaceutical drugs can be tested in humans (i.e. pre-clinical trials).[168] Second, it is unethical to

[161] USEPA 2016. Guidelines for Human Exposure Assessment. Risk Assessment Forum, Peer Review Draft. pg. 12

[162] California Code of Regulations. Division 4.5, Title 22, Chapter 54, Sections 69401-69401: Green Chemistry Hazard Traits for California's Toxics Information Clearinghouse. Available: https://oehha.ca.gov/media/downloads/risk-assessment//gcregtext011912.pdf

[163] Vandenberg, L.N., 2013. Non-Monotonic Dose Responses in Studies of Endocrine Disrupting Chemicals: Bisphenol A as a Case Study. *Dose-Response*, 12(2), pp.259–276.

[164] Zoeller, R.T. & Vandenberg, L.N., 2015. Assessing dose–response relationships for endocrine disrupting chemicals (EDCs): a focus on non-monotonicity. *Environmental Health*, 14(1).

[165] 82 Fed. Reg.7571

[166] IARC Monographs Preamble http://monographs.iarc.fr/ENG/Preamble/

[167] Huff J. Predicting chemicals causing cancer in animals as human carcinogens. Occup Environ Med. 2010 Oct;67(10):720.

Maronpot RR, Flake G, Huff J. Relevance of animal carcinogenesis findings to human cancer predictions and prevention. Toxicol Pathol. 2004 Mar-Apr;32 Suppl 1:40-8. Review.

Huff J. Chemicals and cancer in humans: first evidence in experimental animals. Environ Health Perspect. 1993 Apr;100:201-10. Review.

[168] Page R, Baneux P, Vail D, Duda L, Olson P, Anestidou L, Dybdal N, Golab G, Shelton W, Salgaller M, Hardy C. Conduct, Oversight, and Ethical Considerations of Clinical Trials in Companion Animals with Cancer: Report of a

intentionally expose human subjects to hazardous substances - particularly sensitive or vulnerable populations such as pregnant women, children, and people with pre-existing diseases or other complications. It is for this reason that significant resources are spent to develop animal models to research human diseases. In summary, information from animal experiments remain essential to predictive toxicology, to understand the fundamental mechanisms underpinning adverse outcomes, and to discover improved methods to prevent, diagnose and treat disease.

Epidemiologic data provide critical information about the systemic effects of chemicals under realistic exposure scenarios such as workplace exposures, exposures to pregnant women and reproductive aged men, and exposures to complex mixtures. Epidemiologic studies of populations and individuals can provide not only the most valuable information, but the only available hazard information, about the chemical in people. For example, in 1965, the painful, crippling, degenerative bone disease, acro-osteolysis ("AOL"), was first discovered to be associated with workplace exposures to vinyl chloride.[169] Case reports were published in the medical literature in 1967.[170] The medical case reports led to a key epidemiological investigation in 1969,[171] but unfortunately, it wasn't until 1974-75, when both worker epidemiology and rodent laboratory studies reported that vinyl chloride also caused rare liver cancers in workers.[172] In response, OSHA issued a notice effective 1975 that vinyl chloride and polyvinyl chloride production plants must reduce time-weighted average workplace exposure levels from 500 ppm to 1 ppm, a decade after the first medical reports of AOL among vinyl chloride workers. [173]

The use of biomarkers in epidemiology is a rapidly advancing field, and can indicate molecular, cellular, or other biological events relevant to hazard assessment. For example, biomarkers can provide evidence of exposure, indicate upstream events that precede an adverse outcome, or identify individual susceptibility. This field is integrating with genomics, epigenomics, proteomics, and metabolomics. For example, molecular epidemiological data could help identify a mechanism of toxicity, or help link genetic polymorphisms and interindividual differences in susceptibility to the toxic exposure under study.

Negative epidemiology, when the study shows little or no association between an exposure and an adverse outcome, should not be used to conclude that there is no risk, because epidemiologic studies are designed to 'bias to the null' such that any weaknesses or limitation in the study design will make it more difficult to detect an association if one exists.

In addition, as described in 702.39 (e) (4) (i), although population-based epidemiological studies are a

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Workshop on Best Practice Recommendations. J Vet Intern Med. 2016 Mar-Apr;30(2):527-35.

Workman P, Aboagye EO, Balkwill F, Balmain A, Bruder G, Chaplin DJ, Double JA, Everitt J, Farningham DA, Glennie MJ, Kelland LR, Robinson V, Stratford IJ, Tozer GM, Watson S, Wedge SR, Eccles SA; Committee of the National Cancer Research Institute. Guidelines for the welfare and use of animals in cancer research. Br J Cancer. 2010 May 25;102(11):1555-77.

[169] Markowitz G and Rosner D. 2002. Deceit and Denial: The deadly politics of industrial pollution. Page 176.

[170] Wilson RH, McCormick WE, Tatum CF, Creech JL. Occupational acroosteolysis. Report of 31 cases. JAMA. 1967 Aug 21;201(8):577-81.

[171] Markowitz G and Rosner D. 2002. Deceit and Denial: The deadly politics of industrial pollution. Page 176.

[172] Sass JB, Castleman B, Wallinga D. Vinyl chloride: a case study of data suppression and misrepresentation. Environ Health Perspect. 2005 Jul;113(7):809-12.

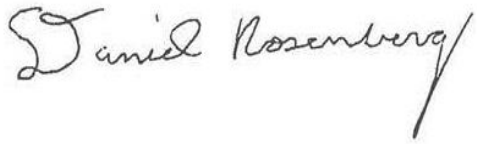
[173] Id.

good resource for identification of risk factors and susceptible populations, this information may not be available for all chemicals and/or uses. The absence of such studies, or findings in the epidemiologic literature, should not be interpreted as the absence of increased risk or susceptibility, and other data sources may be required to identify the relevant exposure patterns for susceptible populations.

Conclusion

The risk evaluation rule, along with EPA's rule on prioritization, is the linchpin of the reformed TSCA program. They will set the ground rules for how some of the most important elements of the TSCA program will operate for years if not decades. Moreover, the content of these ground rules – and the decisions that EPA will make going forward with implementation -- will have profound implications for the health of millions of Americans. To break the cycle of failure that has burdened the TSCA program for so long, it is critical that the Agency finalize these rules within the statutorily mandated deadlines and in a manner that is fully consistent with the underlying law. EPA's proposed risk evaluation rule is fundamentally sound, needing only simple clarifications in a few places to ensure that the rule is consistent with the preamble and the revised statute. NRDC appreciates the opportunity to comment on this important proposal and we look forward to working with EPA to ensure that implementation of the revised TSCA provides the protections for health and the environment the law requires.

Sincerely,



Daniel Rosenberg
Senior Attorney
Natural Resources Defense Council

Veena Singla
Staff Scientist
Natural Resources Defense Council

Attachments

1. Letter from Senators Inhofe, Udall, et al, dated November 30, 2016 to Vice President Elect Mike Pence

United States Senate
WASHINGTON, DC 20510

November 30, 2016

The Honorable Mike Pence
Chair
Presidential Transition Team Executive Committee
1800 F Street NW
Washington, DC 20006

Dear Mr. Vice President-Elect:

As you continue the transition process, we want to highlight for you the implementation of the Frank R. Lautenberg Chemical Safety for the 21st Century Act. This bill to reform the Toxic Substances Control Act (TSCA) of 1976 was signed by the President on June 22, 2016. The badly needed reforms were widely supported in Congress by a 403-12 vote in the House of Representatives and by voice vote in the Senate with near unanimous support. The effort took several years to complete, resulting in the most recent reform of a landmark environmental law since the 1990 Clean Air Act amendments.

TSCA was severely crippled in the 1990s and failed to provide basic health and safety protection for the American public. Uncertainty in the regulatory program also harmed innovation and consumer confidence in everyday products. The reformed law requires the Environmental Protection Agency (EPA) to make many critical decisions in the first months and years of the program, and the Agency has a crucial role to play in ensuring that the promise of the new law is realized. The updated law also directs the Centers for Disease Control to investigate and respond to potential cancer clusters and improve communication and data sharing between local, state and federal governments. Given that this implementation will overlap with the change of Administrations, we want to ensure there is continuity and continued momentum during this critical phase.

Having worked to strengthen and pass the Lautenberg Act in order to help protect children and communities from dangerous chemicals, we are now looking to EPA to vigorously implement the new law. This includes moving expeditiously to identify and address chemicals with the greatest potential impact on public health, especially those affecting vulnerable populations expressly required to be protected in the Act, including pregnant women, children, workers, and other at-risk communities. The EPA announced the first ten chemicals for risk evaluation ahead of schedule. Successful implementation of this law will also help ensure there is certainty and restore confidence in the marketplace for manufacturers, consumer product producers, and the public.

We want to work with you next year to see this bipartisan law succeed. In order for that to happen, we urge that you begin working with the Agency to communicate on critical steps that are underway and to get a full appreciation of the new law's deadlines. We urge that you view appointments, funding and staffing to this office with utmost importance. It is essential to maintain momentum during the Presidential transition and in the early months of the new Administration to ensure that this new law is successful.

Sincerely,

Tom Udall
United States Senator

James M. Inhofe
United States Senator

Cory A. Booker
United States Senator

Shelley Moore Capito
United States Senator

Thomas R. Carper
United States Senator

Mike Crapo
United States Senator

Edward J. Markey
United States Senator

Jeffrey A. Merkley
United States Senator

Sheldon Whitehouse
United States Senator