New Chemicals Decision-Making Framework: *Working Approach to Making Determinations under Section 5 of TSCA*

November 2017

Introduction. This document outlines EPA's approach to making decisions on new chemical notices submitted to EPA under TSCA section 5, as amended by the Frank R. Lautenberg Chemical Safety for the 21st Century Act. The Lautenberg Act amendments to TSCA require that EPA make affirmative determinations on notices received under section 5. The document begins with EPA's general decision framework for new chemicals, and then works through how EPA intends to approach each of the five types of new-chemical determinations required under the statute. As EPA continues to gain experience with new chemicals decision making under amended TSCA, it expects to evolve this working approach to making determinations under section 5.

Overall framework

- New chemicals determinations are made using a risk-based approach, taking into account both hazard and exposure.
- The determinations of "presents unreasonable risk"[1] and "not likely to present unreasonable risk"[2] are made based on sufficient information to conduct a reasoned evaluation.[3] If the Environmental Protection Agency (EPA) does not have sufficient information to conduct a reasoned evaluation, EPA may make a determination of "insufficient information"[4] or "insufficient information and may present unreasonable risk."[5]
- EPA may also make a finding of "substantial production and substantial or significant release or exposure."[6]
- In its reasoned evaluation to determine whether a substance presents or is not likely to present unreasonable risk, EPA considers the potential adverse impact (e.g., severity or reversibility of effect) of the substance and/or its degradation

[1] See Toxic Substances Control Act ("TSCA") § 5(a)(3)(A), 15 U.S.C. § 2604(a)(3)(A).
[2] See TSCA § 5(a)(3)(C), 15 U.S.C. § 2604(a)(3)(C).
[3] Reaching an understanding of what constitutes a *reasoned evaluation* is central to making sound and transparent determinations. A reasoned risk-based evaluation will generally include adequate information to characterize both hazard and exposure, with an ability to shape those characterizations into a quantitative or robust qualitative characterization of risk. While under section 5 both "presents" and "not likely" determinations must be made through a reasoned evaluation, the wording of "presents unreasonable risk" is less equivocal than "not likely to present unreasonable risk." This suggests that the level of uncertainty in a reasoned evaluation to inform a "not likely" determination could be greater than that in an evaluation to inform a "presents" determination.
[4] See TSCA § 5(a)(3)(B)(i), 15 U.S.C. § 2604(a)(3)(B)(i).
[5] See TSCA § 5(a)(3)(B)(ii)(I), 15 U.S.C. § 2604(a)(3)(B)(ii)(I).
[6] See TSCA § 5(a)(3)(B)(ii)(II), 15 U.S.C. § 2604(a)(3)(B)(ii)(II).

products, and the nature of the potential exposures (e.g., duration, magnitude, population, etc.) under the conditions of use, including workplace practices and exposure controls. The evaluation also considers EPA's confidence in the data used in the risk estimate. For instance, if EPA's evaluation indicates a cancer risk based on a particular tumor type seen that is linked to a mechanism of action most relevant or predominant in an animal species (e.g., mediated via PPAR-alpha), how much confidence does EPA have—i.e., what is the likelihood—that the animal data indicate potential risk to humans? The concepts of reasonableness and likelihood are interrelated, and therefore need to be considered together in making a determination.

- In general, EPA considers the intended conditions of use to be the circumstances around manufacture, processing, distribution in commerce, use, or disposal as stated in the submission, original or amended. Such circumstances include engineering controls and other worker protections described in the submission.
- Where the conditions of use identified in submissions raise risk concerns, if the submitters provide timely written amendments to their submissions addressing those concerns, in general EPA will consider the conditions of use in those amended submissions to be the intended conditions of use.[7]
- Where EPA has concerns with reasonably foreseen conditions of use, but not with the intended conditions of use as described in a submission (original or amended), EPA will assess whether those concerns can be addressed through significant new use rules (SNURs). The expectation is that SNURs will generally be effective vehicles to address such concerns and that, as a general matter, EPA will address such concerns through SNURs.
- As described in the risk evaluation rule, the identification of any reasonably foreseen conditions of use will be fact- or knowledge-specific: that is, it will be based on evidence, knowledge, or experience leading EPA to foresee conditions of use different from those described in the submission.[8]

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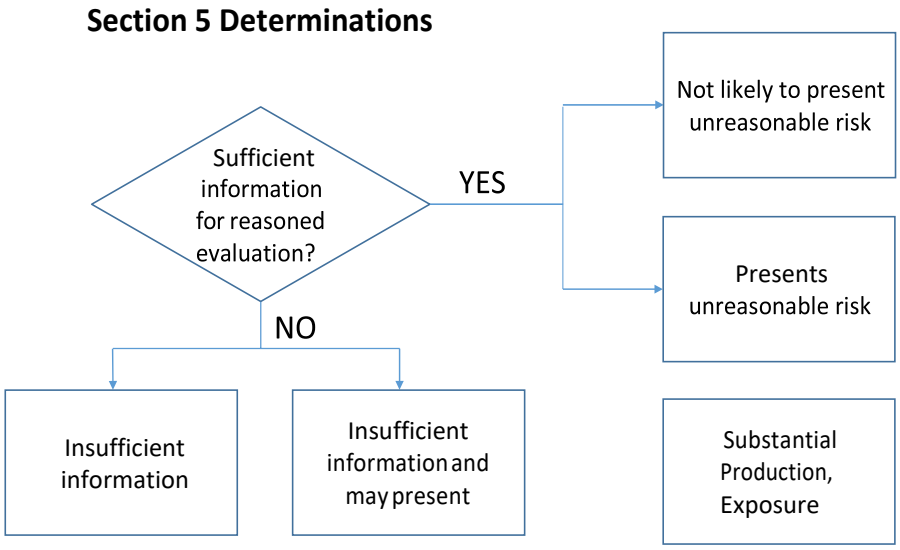
[7] In general, "timely" means early enough in the review process to allow EPA to re-assess risks and make a determination within the applicable review period. In some cases, however, both EPA and the submitter may agree to suspend the review period to allow for a re-assessment.

[8] An example of such knowledge would be information that an analog to the PMN substance (1) has known conditions of use not described in the PMN; and (2) EPA has experience, knowledge or information suggesting it is reasonably possible that the submitter or some other entity could use the PMN substance for the known conditions of use of the analog. Or, for example, EPA may determine that releases to water for the intended use will not exceed the concentration of concern (CoC), but larger releases could result in a CoC exceedance. In this case, it is reasonably foreseen that the CoC could be exceeded. The principle is that EPA should try to minimize speculation when identifying reasonably foreseen conditions of use.

- The purpose of testing in a section 5 order is to reduce uncertainty in making risk determinations. Specifically, it is generally to reduce uncertainty associated with assessments that gave rise to a finding of "may present unreasonable risk" or to an "insufficient information" determination. In addition, consistent with the statute, any request for testing by EPA will be structured to reduce and replace animal testing to the extent practicable and scientifically justified.

Determination-Specific Decision Frameworks

In the following discussions, EPA lays out general principles for making section 5 determinations and some of the factors considered. These discussions are not intended to be interpretations of what is required by TSCA or the range of discretion afforded by TSCA; nor are they a recitation of the elements of a specific determination. In addition, specific cases may present circumstances that are not addressed in these discussions or that warrant different approaches from those set out here.



Presents Unreasonable Risk

- As a result of the review process, EPA concludes that there is sufficient information to conduct a reasoned evaluation. That is, data on the chemical

substance or on analogs are adequate to characterize, with an acceptable degree of certainty, the hazard of the substance and its exposure potential.

- Health or environmental risks under the conditions of use are above risk benchmarks[9]; and
- Risk-related factors—such as severity of endpoint, reversibility of effect, or exposure-related considerations—lead EPA to determine that the risks are unreasonable under the conditions of use.
- EPA's concerns regarding the conditions of use have not been adequately addressed through amendment of the pre-manufacture notice (PMN) made during the review period in conjunction with the issuance of a SNUR, or issuance of a SNUR without amendment of the PMN.

Not Likely to Present Unreasonable Risk

- As a result of the review process, EPA concludes that there is sufficient information to conduct a reasoned evaluation. That is, data are adequate to characterize, with an acceptable degree of certainty, the hazard of the substance and its exposure potential.
- Health and environmental risks for the conditions of use are below our benchmarks; or
- Health and environmental risks are above the appropriate benchmarks, but other risk-related factors—such as severity of endpoint, reversibility of effect, or exposure-related considerations (duration, magnitude, population, etc.)—lead EPA to determine that the risks are not likely to be unreasonable.[10]
- If EPA had concerns regarding the conditions of use, such concerns were adequately addressed through amendment of the PMN made during the review period in conjunction with the issuance of a SNUR, or issuance of a SNUR without amendment of the PMN.

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[9] Benchmarks here means estimated risks above which EPA generally has had concern. For example, a 1×10^{-6} cancer risk estimate has often been considered a "benchmark" above which EPA has concerns for exposure to the general population.

[10] As stated in the risk evaluation final rule, in determining whether there are unreasonable risks, relevant factors include, but are not limited to: the effects of the chemical substance on health and human exposure to such substance under the conditions of use (including cancer and non-cancer risks); the effects of the chemical substance on the environment and environmental exposure under the conditions of use; the population exposed (including any susceptible populations); the severity of hazard (the nature of the hazard, the irreversibility of hazard); and uncertainties in the assessment.

Insufficient Information to Permit a Reasoned Evaluation

- As a result of the review, EPA determines that there is insufficient information to conduct a reasoned evaluation. That is, data (including for the chemical substance, for an analogous substance, from a predictive model, or a structural alert) are inadequate to characterize, with an acceptable degree of certainty, the hazard of the substance, and/or its exposure potential.
- The available information, such as on an analog or a structural alert, is not adequate to determine if there may be potential health or environmental concerns for the substance.
- EPA's concerns regarding the conditions of use have not been adequately addressed through amendment of the PMN made during the review period in conjunction with the issuance of a SNUR, or issuance of a SNUR without amendment of the PMN.

Insufficient Information to Permit a Reasoned Evaluation and May Present Unreasonable Risk

- As a result of the review, EPA determines that there is insufficient information to conduct a reasoned evaluation. That is, data are inadequate to characterize, with an acceptable degree of certainty, the hazard of the substance, and/or its exposure potential.
- However, there is some indication, such as by information on an analog or a structural alert, of potential health or environmental concerns for the substance.
- EPA's concerns regarding the conditions of use have not been adequately addressed through amendment of the PMN made during the review period in conjunction with the issuance of a SNUR, or issuance of a SNUR without amendment of the PMN.

Reasonably Anticipated to be Produced in Substantial Quantities and May Enter the Environment in Substantial Quantities or May be Significant or Substantial Human Exposure

- As a result of the review, and guided by EPA's established criteria, EPA determines that the substance is anticipated to be both produced in substantial quantities *and* be a significant/substantial source of environmental or human exposure or release.
- The statutory consideration of "reasonably be anticipated" should be considered equivalent to "reasonably foreseen" in terms of EPA having the evidence, knowledge, or experience to suggest that this finding is appropriate.