



OMB Control No.: 2070-0038

# Points to Consider When Preparing TSCA New Chemical Notifications

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## Office of Pollution Prevention and Toxics

This document communicates scientific approaches, best practices, and other general guidance that are not binding on either EPA or any outside parties. The document discusses existing statutory and regulatory requirements, but does not create new requirements. The information submission requirements discussed in this document are specified in Agency Premanufacture Notification regulations at 40 CFR part 720. The document also discusses additional information that the Agency recommends companies submit in certain cases. Submission of such information is not required.

This is an evolving document, and EPA has made changes to address public comments. In updating this document, EPA received public input. (See docket EPA-HQ-OPPT-2017-0585 at [www.regulations.gov](http://www.regulations.gov).) Commenters asked many questions that, while not directly relevant to this document, may be useful to submitters. Those comments, questions, and EPA responses can be found at <https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/points-consider-when-preparing-tsca>. While this document includes guidance regarding submissions under Section 5 of TSCA, be aware that the document is not definitive, and EPA may depart from the document at its discretion, in accordance with applicable law.

### **PRA Statement**

This collection of information is approved by OMB under the Paperwork Reduction Act, 44 U.S.C. 3501 et seq., and assigned OMB Control No. 2070-0038. Responses to this collection of information are mandatory for certain persons who engage in the covered activities as specified in section 5 of the Toxic Substances Control Act and EPA implementing regulations (40 CFR parts 720 through 725). An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. The public reporting and recordkeeping burden for this collection of information, which varies based on the activity, is estimated to be between 93 hours per response. Send comments on the Agency's need for this information, the accuracy of the provided burden estimates and any suggested methods for minimizing respondent burden to the Director of Information Engagement Division, Office of Mission Support, U.S. Environmental Protection Agency (2821T), 1200 Pennsylvania Ave., NW, Washington, D.C. 20460. Include the OMB control number in any correspondence. Do not send the completed form to this address.



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## I. PURPOSE AND BACKGROUND

The purpose of this document is to provide information from the United States Environmental Protection Agency (“EPA”) to assist submitters in preparing a Premanufacture Notice (“PMN”), Significant New Use Notice (SNUN)<sup>1</sup>, or exemption notice (*e.g.*, Low Volume Exemption or LVE) (hereinafter collectively referred to as “notifications”) submitted under Section 5 of the Toxic Substances Control Act (TSCA). Following the guidance in this document may (1) help the notifications meet the requirements of TSCA Section 5 and applicable regulations and (2) facilitate EPA’s review of notifications. Following the guidance helps ensure that the information received accurately and completely reflects the intended<sup>2</sup> manufacture, processing, distribution in commerce, use, and disposal of the new chemical substances subject to the Section 5 notice. The information contained in this document can be found, along with more details, in EPA’s Instruction Manual for Reporting Under the Toxic Substances Control Act §5 New Chemicals Program at <https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/instruction-manual-reporting-under>.

New Chemical notification is a requirement under section 5 of the Toxic Substances Control Act (“TSCA”) and corresponding regulations which notifies EPA of a company’s intent to manufacture (which under TSCA includes import) a new chemical substance.<sup>3</sup> PMNs must include data specified in 40 CFR Part 720 and on the PMN form (*i.e.*, EPA Form 7710-25 (Rev. 6-09)), available at: <https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/sample-premanufacture-notification>, regarding chemical identity, impurities, synonyms/trade names, byproducts, production volume (“PV”), uses, and site information including identity, process descriptions, worker exposure information, information on release to the environment, including the quantity and media of release and control technology used. 40 CFR § 720.50 requires submission of test data in the possession or control of the submitter, parent company, or affiliates, which are related to the effects on human health or the environment. Other data concerning the human health and environmental effects of the new chemical substance that are known to, or reasonably ascertainable by, the submitter must also be described by the submitter as part of the PMN. SNUN requirements are specified in 40 CFR § 721.25, and requirements for premanufacture notification exemptions are specified in 40 CFR part 723.

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<sup>1</sup> While the discussion regarding data to be submitted and EPA’s review and analysis applies equally to review of PMNs, SNUNs and exemption applications, for simplicity’s sake this discussion will refer to PMNs.

<sup>2</sup> EPA welcomes any information that submitters can provide on the conditions of use associated with reasonably foreseen uses. Since in most cases submitters will have limited information regarding reasonably foreseen uses, the Points to Consider document focuses on information that may inform EPA’s evaluation of intended uses (*i.e.*, those identified in the notification and any amendments). As stated in EPA’s *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act*, the identification of ‘reasonably foreseen’ conditions of use will necessarily be a case-by-case determination, and will be highly fact-specific. See: Federal Register (2017), Vol. 82, pp. 7562-7580.

<sup>3</sup> SNUNs are submitted pursuant to a Significant New Use Rule (SNUR) promulgated under TSCA § 5(a)(2) by companies that manufacture or process for the Significant New Use described in the SNUR.

Under section 5(h) of TSCA, EPA either grants or denies exemption notifications according to 40 CFR 720.38, 40 CFR part 723 and section 5(h)(4) of TSCA.

Under section 5(a)(3) of TSCA, EPA determines that either

- (1) the new chemical substance or significant new use presents an unreasonable risk of injury to human health or the environment (§5(a)(3)(A)),
- (2) the information on the new chemical substance or significant new use is insufficient to make a reasoned evaluation of the health and environmental effects (§5(a)(3)(B)(i)),
- (3) in the absence of sufficient information the new chemical substance may present an unreasonable risk of injury to health or the environment (§5(a)(B)(ii)(I)),
- (4) the new chemical substance is or will be produced in substantial quantities, and such substance either enters or may reasonably be anticipated to enter the environment in substantial quantities or there is or may be significant or substantial human exposure to the substance (§5(a)(B)(ii)(II)), or
- (5) the new chemical substance or significant new use is not likely to present an unreasonable risk of injury to human health or the environment (§5(a)(3)(C)).

These determinations are the result of EPA's New Chemical Review process. Useful discussion of EPA's assessment models and methods can be found in EPA's Sustainable Futures/P2 Framework Manual, available at: <https://www.epa.gov/sustainable-futures/sustainable-futures-p2-framework-manual>.

EPA regulations require certain information from submitters when they complete and file notifications with the Agency (see, *e.g.*, 40 CFR parts 720 and 723). If required information is not submitted as part of the notification, EPA may declare the notice to be incomplete and the review period will not begin. If sufficiently specific information is lacking, EPA typically makes conservative assumptions, which oftentimes lead to the practice of delayed reviews and frequent suspensions while submitters work with the Agency to provide and/or develop additional information. This document is intended to reduce the frequency of such delays.

EPA has identified two basic scenarios that often lead to delays in reviewing notifications in the New Chemical Review process:

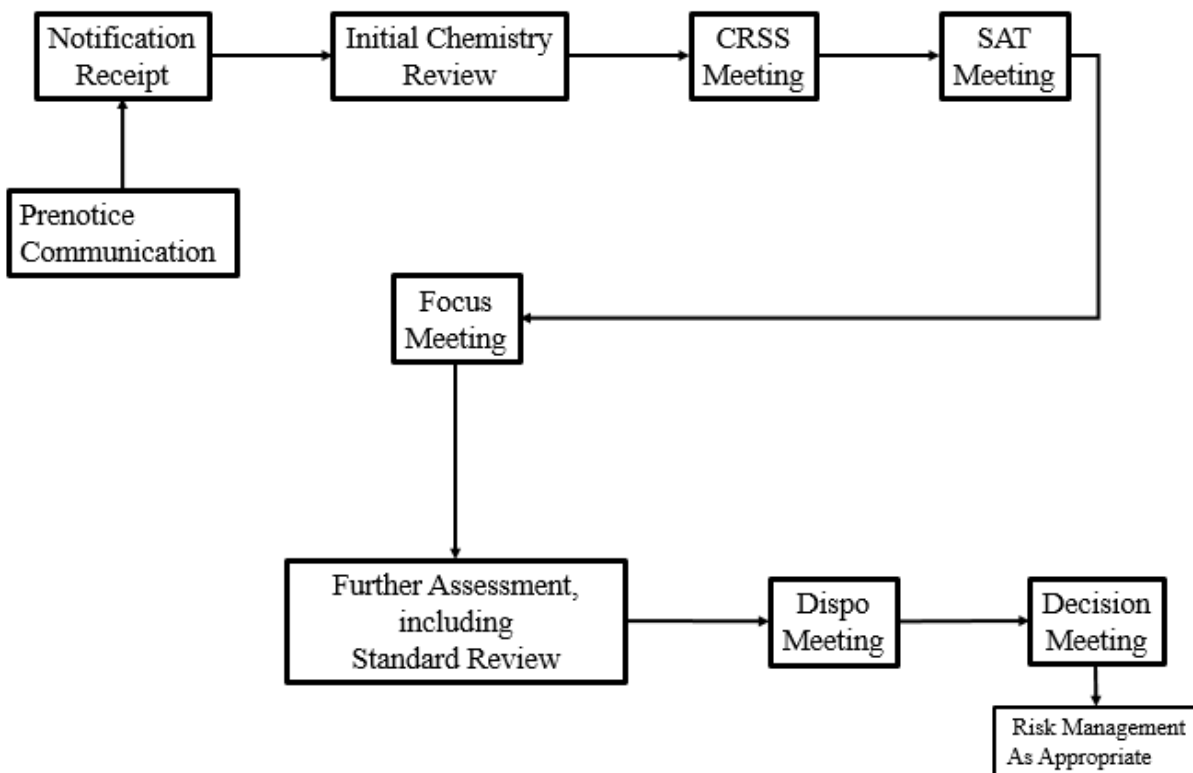
- (1) The provided information lacks specific details, which precludes EPA from using the information in lieu of generally conservative assumptions, and
- (2) Additional information, which would aid EPA with refining its assumptions, are not provided by the submitter in the original notice, are not in the possession or control of the submitter, or are not generated until after the initiation or completion of the New Chemical Review process.

Notifications that lack detail typically result in follow-up or additional interaction with submitters, which in turn, adds time to the New Chemical Review process. If the submitter provides additional information, EPA will generally conduct additional analyses and/or re-evaluate the notification in light of the additional information. In an effort to ensure that

notifications are not delayed, EPA encourages submitters to review and to consult this document while preparing their notifications, so they understand the utility of submitting complete information with the original submission.

The information provided in this document provides an overview of the New Chemical Review process and how EPA evaluates notifications. The format is to begin with a description of information required to be submitted to EPA electronically via the Internet using EPA's Central Data Exchange (CDX)) on EPA Form 7710-25 (Rev. 6-09) (see: <https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/sample-premanufacture-notification>), then to describe each step of the New Chemical Review process, as shown in the following diagram, and finally, to provide recommendations on types of information and/or specificity of information that will facilitate a more refined evaluation of new chemical substances.

## Overview of the New Chemical Review Process<sup>a</sup>



<sup>a</sup> Abbreviations: CRSS = Chemistry Review and Search Strategy; SAT = Structure-Activity Team; Dispo Meeting = Disposition Meeting

## II. GENERAL INFORMATION REQUIREMENTS FOR NOTIFICATIONS

The information in this section is required by 40 CFR part 720 to be entered on EPA Form 7710-25 (Rev. 6-09). If there is not a section on the form to enter the information, it must be provided to EPA as an attachment. Note: Citations to the Code of Federal Regulations (CFR) are made where specific types of information are required; however, these only serve as examples. Submitters should read the relevant regulatory provisions to ensure submissions comply with all the information requirements, prior to submitting a notification to the New Chemical Review process.

### A. *Chemical Identity and Physical-Chemical Property Information*

The New Chemical Review process requires an accurate depiction of the chemical identity and molecular structure (or representative structure(s)) and description of physical-chemical properties of the chemical substance. The presence of functional groups and basic physical-chemical properties of a chemical substance are used by EPA to determine what hazards and exposure pathways may be expected and relevant for the chemical substance. This information is also used to determine if a chemical substance belongs in one of EPA's established TSCA New

Chemicals Program Chemical Categories.<sup>4</sup> Guidance to follow to avoid submitting an incomplete PMN can be found at: <https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/guidance-avoiding-incomplete>.

*Submitters are required to provide the following information on EPA Form 7710-25 (Rev. 6-09).*<sup>5</sup>

- A correct Chemical Abstracts (“CA”) Index name. *See, e.g.*, 40 CFR 720.45(a)(1)(i).
- Consistent chemical identity information throughout the notification. For example, submitters are required to make sure that the chemical identity on page 4 of EPA Form 7710-25 (Rev. 5-95) matches the manufacturing diagram.
- Information on polymers on page 5 of EPA Form 7710-25 (Rev. 5-95). *See, e.g.*, 40 CFR § 720.45(a)(2).
- As much structurally descriptive information as possible for chemical substances of unknown or variable compositions, complex reaction products and biological materials (“UVCBs”).
- A generic name that is only as generic as necessary to protect the confidential chemical identity of the new chemical substance. The name should reveal the specific chemical identity to the maximum extent possible. *See*, TSCA Section 14(c)(1)(C), 40 C.F.R. § 720.85(a)(2)(ii), and <https://www.epa.gov/tsca-inventory/instructions-developing-generic-names-premanufacture-notice-pmns-tsca-inventory>.

## ***B. Domestic Production, Import, and Use Information***

*Submitters are required to provide the following information on EPA Form 7710-25 (Rev. 5-95).*<sup>6</sup>

- An estimate of the expected maximum 12-month PV to be manufactured (includes both domestic production and import) during any 12-month period during the first three years of production. Submitters are required to avoid underestimating, as this may influence future activity depending on the results of the risk evaluation. *See, e.g.*, 40 CFR § 720.45(e).
- The expected percentage of total chemical substance PV for the first three years of production for each category of use. For example, 50% of the PV will be used for coatings and 50% of the PV will be used for inks. *See, e.g.*, 40 CFR § 720.45(e).
- Appropriate product and/or article use categories and functional use categories for the chemical substance<sup>7</sup>. *See, e.g.*, 40 CFR § 720.45(f).

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<sup>4</sup> EPA’s established TSCA New Chemical Program Chemical Categories can be found at: [https://www.epa.gov/sites/production/files/2014-10/documents/ncp\\_chemical\\_categories\\_august\\_2010\\_version\\_0.pdf](https://www.epa.gov/sites/production/files/2014-10/documents/ncp_chemical_categories_august_2010_version_0.pdf).

<sup>5</sup> See generally, 40 CFR § 720.45 “Information that must be included in the notice form”

<sup>6</sup> *Id.*

<sup>7</sup> The OECD Working Party on Exposure Assessment (TFEA) has developed guidance documents for reporting releases, use of exposure models, reporting monitoring information, and reporting exposure information (<http://www.oecd.org/env/ehs/risk-assessment/oecdactivitiesonexposureassessment.htm>). Definitions of use codes, emission scenario documents, and additional guidance will be posted to this website over time.



- Specific percent of total PV of the chemical substance used for all uses described in the notification. *See, e.g.*, 40 CFR § 720.45(f).
- Specific concentrations (weight fraction) used in all consumer applications. *See, e.g.*, 40 CFR § 720.45(f).
- The identity of all sites controlled by the submitter where the chemical substance will be manufactured, processed, or used. *See, e.g.*, 40 CFR § 720.45(g)(1).
- Accurate estimates (in ranges) of the number of manufacturing, processing and use sites. *See, e.g.*, 40 CFR § 720.45(g)(2).
- A process description of each manufacture, processing, and use operation controlled by the submitter, including a diagram of the major unit operations and chemical conversions, the identity and entry point of all feedstocks, and the points of release of the chemical substance. *See, e.g.*, 40 CFR § 720.45(g)(2). Accurate representation of the process aids EPA in determining potential release and exposure points and improves the accuracy and overall quality of the engineering assessment.
- Worker exposure information at all sites controlled by the submitter, including worker activities, physical form of the chemical substance to which workers may be exposed, the number of workers, and the duration of activities. *See, e.g.*, 40 CFR § 720.45(g)(3).
- Information on release of the new chemical substance to the environment, including the quantity and media of release and type of control technology used. *See, e.g.*, 40 CFR § 720.45(g)(4).
- A description of each type of processing and use operation involving the chemical substance for sites not controlled by the submitter, including identification of the estimated number of processing or use sites, situations in which worker exposure to the chemical substance will occur, the number of workers exposed and the duration of exposure, and controls which limit worker exposure. *See, e.g.*, 40 CFR § 720.45(h).

### ***C. Test Data***

*Submitters are required to provide the following data in their possession or control on the chemical substance:*<sup>8</sup>

- All test data in the submitter’s possession or control which are related to the effects on health or the environment of any manufacture, processing, distribution in commerce, use, or disposal of the new chemical substance or any mixture or article containing the new chemical substance, or any combination of such activities. This includes test data concerning the new chemical substance in a pure, technical grade, or formulated form. *See, e.g.*, 40 CFR § 720.50(a)(1).
- A full report or standard literature citation for the following types of test data (*See, e.g.*, 40 CFR § 720.50(a)(2):
  - Health effects data.
  - Ecological effects data.
  - Physical and chemical properties data.

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<sup>8</sup> See generally, 40 CFR § 720.50 “Submission of test data and other data concerning the health and environmental effects of a substance”

- Environmental fate characteristics.
  - Monitoring data and other test data related to human exposure to or environmental release of the chemical substance.
- Completed full study reports. *See, e.g.,* 40 CFR § 720.50(a)(3)(i).

In addition to providing the required test data, submitters may consider providing full study reports, if available, of any other test data the submitter considers to be important for EPA to consider, e.g., test data on analogs. Providing full studies streamlines the review process and allows EPA assessors to determine study quality, completeness and suitability and to evaluate study outcomes.

### **III. THE NEW CHEMICAL REVIEW PROCESS AND THE IDENTIFICATION OF ADDITIONAL INFORMATION THAT CAN EXPEDITE AND REFINE THE REVIEW**

#### ***A. Pre-Notice Consultation***

Pre-notice Consultation meetings cover topics related to the preparation of a notification and the completeness of a notification to enter the New Chemical Review process. These meetings are not intended to obtain EPA decisions on the content and likely outcome from the New Chemical Review process. For example, EPA will not make a determination at a Pre-notice Consultation meeting on whether there may or may not be potential risks to human health and/or environmental receptors, nor will EPA make a risk management finding (*e.g.*, not likely, may present, or will present).

Prior to requesting a Pre-notice Consultation, submitters should review the Points to Consider document. Many of the questions that EPA receives during Pre-notice Consultation meetings are addressed in this document, and submitters may determine after reading this document that a Pre-notice Consultation meeting is not necessary. If submitters still have questions about their notifications, Pre-notice Consultations generally consist of the following steps:

- Initial Request for a Pre-notice Consultation meeting
  - EPA encourages submitters to submit a written request to EPA's Chemical Control Division. The request will ideally include the following types of information:
    - Identity of the chemical substance,
    - Type of submission (*e.g.*, PMN, SNUN, or an exemption),
    - Description of proposed and reasonably foreseeable uses,
    - A list of issues the submitter wishes to raise for EPA's consideration, and
    - Summary of any previous discussions involving EPA staff on the issues
- Timing for EPA's response and determination on the necessity of a Pre-notice Consultation meeting
  - EPA generally responds to Pre-Notice Consultations within two to four weeks of receipt.
  - Following receipt, EPA will discuss with the requester whether a written response or meeting/teleconference is preferred.
- Conduct of the Pre-notice Consultation meeting
  - The meeting may take place by telephone or in person, depending on the submitters' location and availability.
  - EPA will take notes during the meeting and will record who attended.
  - The meeting length should generally be from one to no more than two hours in length, although many Pre-notice Consultation meetings are completed in less than an hour.

- EPA will respond to the submitter's questions about EPA's initial written responses on the submitter's issues and will clarify those responses to the extent possible during the meeting.
- Summary of the Meeting
  - Upon request, within 10 working days of the Pre-notice Consultation meeting, EPA will provide a set of minutes to the submitter that describes the matters that were discussed, any commitments made by EPA or the submitter, and any conclusions reached at the meeting.

### ***B. Initial Chemistry Review***

Following receipt of a notification, the Initial Chemistry Review is conducted. EPA reviews the notification for completeness—that is, to ensure that required information in specific sections of EPA Form 7710-25 (Rev. 5-95) is provided.

### ***C. Chemical Review and Search Strategy (“CRSS”) Meeting***

Hazard and exposure assessments are informed by the physical-chemical properties of a chemical substance. The CRSS meeting of the New Chemical Review process includes an examination of the following:

- TSCA Inventory status;
- chemical identity;
- structure/chemical nomenclature;
- structural analogs;
- synthesis (including byproducts and impurities);
- use as provided in the notification, identified in an open literature search, or as identified by EPA for similar chemical substances, including whether the use is regulated by TSCA;
- physical-chemical properties (*e.g.*, physical state, molecular weight, melting and boiling point, vapor pressure, solubility, octanol water partition coefficient, pH); and
- pollution prevention aspects,<sup>9</sup> using information provided in the notification.

Decisions at the CRSS meeting include notice completeness, validity, eligibility for exemption or exclusion, and candidacy for exposure-based review (*i.e.*, PV greater than 100,000 kg/year).

The hierarchy of data sources EPA uses to determine physical-chemical property data is as follows, with the most reliable source listed first:

- Measured values from submitters or primary references.

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<sup>9</sup> For more information, see: New Chemicals and Pollution Prevention Efforts, Reviewing New Chemicals under the Toxic Substances Control Act, available at: <https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/new-chemicals-and-pollution>

- Estimated values based on chemical analogs.<sup>10</sup>
- Estimated values generated using computer models.<sup>11</sup>
- Estimated values based on common chemical structure or type.

*EPA often receives notifications where the following types of relevant information have not been generated, prior to submitting the notification:*

- Measured values for the chemical substance including basic physical-chemical properties (e.g., water solubility, vapor pressure, melting point, and octanol/water partition coefficient).
  - In the absence of data, EPA will generally utilize chemical analogs and/or computer models to estimate these properties.<sup>12</sup>
- Particle size distribution or droplet size analysis data if the chemical substance is manufactured or processed as a particulate or used in aerosolized spray applications. EPA will often have particular concerns for respirable particles/droplets less than 10 µm (micrometers) that have the potential to enter the deep lung. The particle size distribution analysis should be based on the form of the substance to which the workers may be exposed, e.g., post-transport.
  - In the absence of data, EPA will generally assume the chemical substance is respirable.
- The concentration of the dissociated (ionized) and undissociated (neutral) forms of an acid, base, or organic salt in water. The degree of ionization or dissociation may have a substantial impact on the resulting risk assessment.
  - In the absence of data, EPA will generally assess a worst-case scenario—for toxicity, fate, and exposure.

Consideration of whether the chemical substance qualifies for the polymer exemption. A formal commitment, by the submitter, to adhere to the conditions of the polymer exemption (see 40 CFR § 723.250) could allow the chemical substance to be included on the TSCA Inventory with a regulatory flag, once the company has sent the Notice of Commencement (“NOC”). [NOTE: Special flags are used throughout the TSCA Inventory to identify those substances on the Inventory that are the subject of an EPA rule or order promulgated under TSCA, as well as to indicate types of full or partial exemptions from TSCA reporting requirements.] This would expedite the review process, if EPA’s finding on the notification is “not likely to present an unreasonable risk.”

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<sup>10</sup> For more information, see: EPA (2012) 3. *Getting Started by Identifying Existing Data*, Sustainable Futures / P2 Framework Manual, EPA-748-B12-001, available at: <https://www.epa.gov/sites/production/files/2015-05/documents/03.pdf>

<sup>11</sup> For more information, see: EPA (2012) 5. *Estimating Physical / Chemical and Environmental Fate Properties with EPI Suite™*, Sustainable Futures / P2 Framework Manual, EPA-748-B12-001, available at: <https://www.epa.gov/sites/production/files/2015-05/documents/05.pdf>

<sup>12</sup> The predictive methods that EPA has developed to screen chemical substances include expert systems, *in silico* methods, analog analysis and read across, among other approaches. EPA also has access to additional information that cannot be made public because it is protected as “confidential business information” (“CBI”) under TSCA.

## ***D. Structure Activity Team (“SAT”) Meeting***

At the SAT meeting, an interdisciplinary team of chemists, biologists, toxicologists, and information specialists evaluate test data on the new chemical substance (when available), data on analogs, and structure activity relationships (SARs) to formulate initial characterizations on Human Health Hazard/Toxicity, Environmental Fate, and Aquatic (Environmental) Hazard/Toxicity. Below is a summary of the New Chemical Review processes employed to identify and summarize the available data for each of these assessment components prior to the SAT meeting. The discussion begins with how EPA performs its evaluation for each of these components, followed by types of information submitters may consider to facilitate EPA’s review of the new chemical substance.

### **i. Human Health Hazard/Toxicity**

EPA evaluates hazard endpoints both qualitatively (*e.g.*, irritation, respiratory sensitization, mutagenicity), as well as quantitatively (*e.g.*, points of departure from experimental studies), when data are available. The purpose of the human health hazard/toxicity evaluation is to preliminarily characterize or identify the following in preparation for the SAT meeting:

- Absorption by the relevant exposure routes.
  - In the absence of submitted experimental absorption data, the SAT uses absorption data from analogs, or physical-chemical properties [*e.g.*, vapor pressure, water solubility, molecular weight, and log Kow] to provide a qualitative estimate of absorption [*e.g.*, nil, poor, moderate, or good].
  - When no data are available—for the chemical substance or an analog—EPA may assume, based on the properties of the new chemical substance, that absorption could be 100% by any/all routes.
- Potential hazards associated with the new chemical substance based on data provided with the notification.
- Confirm selection of analogs<sup>13</sup> for informing the identification of potential hazard(s).
- Hazard key words for the new chemical substance (*e.g.*, irritation, sensitization, or lung overload). The SAT also reviews safety data sheets provided by the submitter for their characterization of hazard key words.
- Relevant routes of exposure (*e.g.*, dermal, inhalation, fish ingestion, and/or drinking water).

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<sup>13</sup> Information on selection of analogs is available from the following resources:

EPA (2012) 9. *Analog Identification Methodology (AIM)*, Sustainable Futures / P2 Framework Manual, EPA-748-B12-001, <https://www.epa.gov/sites/production/files/2015-05/documents/09.pdf> and <http://www.oecd.org/chemicalsafety/risk-assessment/groupingofchemicalschemicalcategoriesandread-across.htm>

- The human health score (low = 1, moderate = 2, or high = 3); a hazard value greater than 1 will initiate the engineering and exposure assessments (note, an ecotoxicity hazard score greater than 1 will also initiate these assessments), The human health score is typically based on qualitative considerations such as hazard endpoints<sup>14</sup>. For example, endpoints such as developmental/reproductive toxicity or carcinogenicity may lead to scores higher than 1.
- Potential for toxicity (“T”) for the overall persistent (“P”), bioaccumulative (“B”), and toxicity (“PBT”) score. The “T” score is numeric, but is determined qualitatively; a score of 2 is needed for P, B, and T to designate the new chemical substance as a PBT [*i.e.*, P2B2T2 → PBT]).
  - The T score (in the overall PBT score) is based on developmental/reproductive and/or chronic hazards to the general population, and/or to chronic hazards to aquatic organisms (see Section III(C)(iii)); it is not designated for acute toxicity (*i.e.*, mammalian or aquatic organisms) and is not typically used for hazards identified by the dermal or inhalation routes of exposure, as these types of toxicity and exposure routes are not typically associated with P and B chemicals.

When making the above determinations, EPA reviews new chemical substances in the following manner:<sup>15, 16, 17, 18</sup>

- Review structure, physical-chemical properties, and structural alerts.
  - Consider molecular shape and size, fundamental physical-chemical properties, presence and position of reactive functional groups, charge density, minimum cross-sectional diameter of molecules, octanol/water partition coefficients, potential for absorption, metabolic pathways, species sensitivity, and mechanisms of toxicity.
  - Consider potential metabolites or degradates.

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<sup>14</sup> Information on structural alerts is available here:

<sup>15</sup> For more information, see: EPA (2012) 8. *Non-Cancer Human Health Hazard Screening Protocol*, Sustainable Futures / P2 Framework Manual, EPA-748-B12-001, available at: <https://www.epa.gov/sites/production/files/2015-05/documents/08.pdf>

<sup>16</sup> For more information, see: EPA (2012) 9. *Analog Identification Methodology (AIM)*, Sustainable Futures / P2 Framework Manual, EPA-748-B12-001, available at: <https://www.epa.gov/sites/production/files/2015-05/documents/09.pdf>

<sup>17</sup> For more information, see: EPA (2012) 10. *Predicting Carcinogenicity Potential Using OncoLogic™*, Sustainable Futures / P2 Framework Manual, EPA-748-B12-001, available at: <https://www.epa.gov/sites/production/files/2015-05/documents/10.pdf>

<sup>18</sup> For more on exposure-based testing, see: <https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/exposure-based-policy-under-section>

- Determine if chemical (or metabolite or degradate) fits within a TSCA New Chemicals Program Chemical Category<sup>19</sup>, or if the structure contains structural alerts for toxicity<sup>20</sup>.
  - Identify hazards associated with the category and/or structural alerts.
- Review submitted data.
  - Identify hazards associated with or addressed by the submitted data.
  - Determine if the data are suitable for the identification of a point of departure (*e.g.*, no observed adverse effect level [NOAEL], lowest observed adverse effect level [LOAEL], or benchmark dose lower bound [BMDL]) for quantitative risk estimation, or if they can be used for qualitative risk estimation (*e.g.*, sensitization data).
- If there is a Sustainable Futures submission, or other information, such as a review by another international agency, review hazard information for data on the submitted chemical, an analog, or models.
  - Identify hazards associated with or addressed by the submitted data.
  - Determine if the data are suitable for the identification of a point of departure (*e.g.*, NOAEL, LOAEL, or BMDL) for quantitative risk estimation, or if they can be used for qualitative risk estimation.
- Check for analogs. This step is often necessary even if toxicity data are submitted because: submitted data may not address a hazard concern identified based on chemical structure (*e.g.*, category<sup>21</sup> or structural alert) or the submitted data are for a route of exposure other than those relevant for the new chemical substance.
  - Analogs suggested by submitter,
  - Analogs identified during CRSS,
  - Search for analogs using AIM,<sup>22</sup> ChemID*plus* Advanced,<sup>23</sup> OECD QSAR Toolbox,<sup>24</sup> *etc.*
- Determine (based on data) or estimate (based on physical-chemical properties) absorption by route of exposure (*i.e.*, inhalation, dermal, and/or oral).
- Considering totality of available data:
  - Determine hazards associated with the chemical substance.

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<sup>19</sup> For more information, see: EPA (2010) TSCA New Chemicals Program (NCP) Chemical Categories, Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency, Washington, D.C., 157 pp., available at: [https://www.epa.gov/sites/production/files/2014-10/documents/ncp\\_chemical\\_categories\\_august\\_2010\\_version\\_0.pdf](https://www.epa.gov/sites/production/files/2014-10/documents/ncp_chemical_categories_august_2010_version_0.pdf)

<sup>20</sup>Information on structural alerts is available here: <http://www.oecd.org/chemicalsafety/risk-assessment/guidancedocumentsandreportsrelatedtoqsars.htm>

<sup>21</sup> EPA (2010) *supra* note 16.

<sup>22</sup> The Analog Identification Methodology (AIM) Tool is publicly available software, that is available for download at the following: <https://www.epa.gov/tsca-screening-tools/analog-identification-methodology-aim-tool>

<sup>23</sup> ChemID*plus* Advanced is an online TOXNET Database maintained by the U.S. National Library of Medicine, available at the following: <https://chem.nlm.nih.gov/chemidplus/>

<sup>24</sup> The OECD QSAR Toolbox is publicly available software, that is available for download at the following: <http://www.oecd.org/chemicalsafety/risk-assessment/oecd-qsar-toolbox.htm>



- Provide hazard summary.
- Identify points of departure suitable for use in risk assessment and the basis for their selection.

*EPA recommends submitters consider the following information on the chemical substance:*

- In general, EPA will consider the following types of information as part of the New Chemical Review process. If the submitter concludes that any or all of this information is not applicable or relevant to the new chemical substance, providing an explanation or rationale for why such toxicity information is not relevant for the intended use of the chemical substance could inform and expedite EPA's evaluation.
  - Information related to potential human health hazards from short-term exposures.
  - Information related to potential human health hazards from long-term exposures.
  - For experimental data, identify what is considered to be the NOAEL, LOAEL, no observed adverse effect concentration ("NOAEC"), or lowest observed adverse effect concentration ("LOAEC") and explain the rationale (endpoint/measure) for identifying these benchmarks.
- Submitters should consider whether the new chemical substance has been submitted to/reviewed by another international agency (*e.g.*, Health or Environment and Climate Change Canada, European Chemicals Agency, National Industrial Chemicals Notification and Assessment Scheme, *etc.*). If so, it could be useful to provide those submissions and/or supporting information with the PMN.
- Submitters should consider whether the structure of the new chemical substance has any structural alerts<sup>25</sup> (*e.g.*, mutagenicity, oncogenicity, sensitization, and/or reproductive/developmental toxicity). Many of these "alerts" are well recognized/established and required as part of classification and labelling in other jurisdictions, hence providing this information can inform EPA's review.
- For any new chemical substance that may potentially be respirable (either as particulates, liquids, mists, or aerosols), the default assumption is that the chemical substance is respirable. Submitted particle size/droplet size information for the new chemical substance would aid the assessment of respirability.
- Given the language in amended TSCA pertaining to alternative test methods (TSCA Section 4(h)(2)(A)), submitters should consider whether *in silico*, *in vitro*, or other non-vertebrate test information are appropriate for evaluating their chemical substance. This should include appropriate documentation of the method used to generate the data and a clear description of results and what they mean for hazard/risk analysis.
- Submitters should consider whether there are acceptable analog(s) for any toxicity endpoint to support the New Chemical Review process. Analog data may be useful to provide multiple lines of scientific evidence for a determination of hazard concerns, when for example, the hazard concern is identified for a route of exposure (*e.g.*, inhalation) other than the route of exposure (*e.g.*, dermal) for which data are available for the new chemical substance.

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<sup>25</sup> Guidance documents on the identification and use of structural alerts can be found at: <http://www.oecd.org/chemicalsafety/risk-assessment/guidancedocumentsandreportsrelatedtoqsars.htm>

- Provide justification for consideration of the analog for the endpoint(s) identified (e.g., similarity of structure, physical chemistry, toxicological data, as applicable)<sup>26</sup>.
- Provide chemical name and CAS numbers of all analogs.
- Provide clear structural representation of the analog substance(s). It is best to provide a visual representation of the molecular structure along with that of the chemical substance. If EPA cannot determine the molecular structure or composition of the analog, it will not be considered.
- Provide full studies on the analogs, if available, to better ensure efficient consideration by EPA.

## ii. Environmental Fate

Environmental fate data provide significant insight into other components of the New Chemicals Review process such as potential environmental partitioning to various media (air, soil, water, sediment) and potential degradation rates (persistence) in each of those media. Basic fate properties also allow EPA to focus the chemical substance assessment on relevant routes of exposure for workers, consumers, the general population, and environmental receptors. The purpose of the Environmental Fate evaluation is to preliminarily characterize the following in preparation for the SAT meeting:

- Environmental partitioning.
- Potential for persistence (“P”) and bioaccumulation (“B”), use the following general criteria<sup>27</sup> (note, if a new chemical substance is designated as P2B2 or greater, all routes of release and exposure are assessed, regardless of the human health or ecotoxicity hazard score).<sup>28, 29</sup>

Persistence <sup>a</sup>	Low Persistence (P1)	Persistent (P2)	Very persistent (P3)
Water, soil, sediment	< 60 days	≥ 60 days	> 180 days
Air	≤ 2 days	> 2 days	

<sup>26</sup> Information on selection of analogs is available from the following resources:

EPA (2012) 9. *Analog Identification Methodology (AIM)*, Sustainable Futures / P2 Framework Manual, EPA-748-B12-001, <https://www.epa.gov/sites/production/files/2015-05/documents/09.pdf> and <http://www.oecd.org/chemicalsafety/risk-assessment/groupingofchemicalschemicalcategoriesandread-across.htm>

<sup>27</sup> EPA (1999) *Category for Persistent, Bioaccumulative, and Toxic New Substances, Policy Statement*, Federal Register, Vol. 64, No. 213, pp. 60194-60204.

<sup>28</sup> For more information, see: EPA (2012) 7. *Estimating Persistence, Bioaccumulation, and Toxicity Using the PBT Profiler*, Sustainable Futures / P2 Framework Manual, EPA-748-B12-001, available at: <https://www.epa.gov/sites/production/files/2015-05/documents/07.pdf>

<sup>29</sup> Note, EPA also uses information on physical-chemical properties (e.g., logK<sub>ow</sub>), chemical groups (e.g., metals, nanomaterials, perfluorinated compounds, UVCB), etc., to inform the P and B call.

<b>Bioaccumulation<sup>a</sup></b>	<b>Low bioaccumulation (B1)</b>	<b>Bioaccumulative (B2)</b>	<b>Very bioaccumulative (B3)</b>
Fish BCF or BAF	< 1,000	≥ 1,000	≥ 5,000

<sup>a</sup> Note, qualitative estimates based on modeling and/or physical-chemical properties are also used to inform the P and B score.

- Relevant routes of exposure.

When making the foregoing characterizations, EPA reviews new chemical substances in the following manner:

- Review submitted data.
  - Data from studies performed according to validated test guidelines and under Good Laboratory Practice (GLP) standards or non-guideline non-GLP studies which are sufficiently documented to allow EPA to reconstruct and re-evaluate the experimental methods and data are normally considered to be the most appropriate for use in fate assessments.
- Identify suitable analogs.
  - EPA also evaluates analogs with measured data from previous new chemical substance submissions and databases of publicly available literature. If analog information is available for an appropriate chemical or group of chemicals, then this information is used instead of modeled estimates (see below).
- Use modeling to estimate fate parameters.
  - Due to the absence of submitted or analog data, EPA often relies on modeling of the fate properties for new chemical substances using EPISuite<sup>TM</sup>.<sup>30</sup>
  - Each of the various models within EPISuite<sup>TM</sup>, like all models, has a domain of applicability; that is, the models are only useful/accurate for certain chemical groups. Applicability domains include cut-offs, often based on molecular weight and chemical composition/moieties that inform the reliability of the model for various chemicals, (e.g., chemical substances with a molecular weight greater than 1,000 Daltons and inorganic and organometallic chemicals are generally outside the domain of EPISuite<sup>TM</sup>).
  - EPA assesses biodegradation rate information conservatively based on the outputs of the MITI models within the BIOWIN<sup>TM</sup> model of EPISuite<sup>TM</sup>. The MITI model is built on measured information from ready biodegradation testing. EPA considers this the most relevant model in EPISuite<sup>TM</sup> for informing persistence and sewage treatment plant removal rates.
  - EPISuite<sup>TM</sup> does not generate direct photolysis rates, but it does calculate indirect photolysis rates. These are used to estimate atmospheric half-lives and contribute to the persistence call.
  - The rate estimates for biodegradation, persistence, and indirect photolysis are used for designating the P score.

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<sup>30</sup> EPISuite<sup>TM</sup> is publicly available software, that is available for download at the following: <https://www.epa.gov/tsc-screening-tools/epi-suitetm-estimation-program-interface>

- Transport and partitioning parameters are assessed using EPISuite™.
- Where applicable, EPA uses the BCFBAF™ model from EPISuite™ to inform the B score. A conservative approach is used to evaluate the outputs of the BCF regression model and the Arnot-Gobas model within BCFBAF™ (*i.e.*, the higher output of the two models is commonly used to inform the B score). The BCF regression model does not incorporate metabolism for a particular chemical structure and this may result in a higher estimated BCF value than the Arnot-Gobas model, which does include a metabolism rate QSAR. For the Arnot-Gobas model to outweigh the BCF regression model and reduce a B score, the structural components of the new chemical substance need to be well represented in the metabolism QSAR.
- Use physical-chemical properties to estimate fate parameters.
  - If the new chemical substance is not suitable for modeling, then the fate determinations are estimated based on the physical-chemical properties.

*EPA recommends submitters consider the following information on the chemical substance:*

- EPA will consider the following types of information during the New Chemical Review process. If the submitter concludes that any or all of this information is not applicable or relevant to the new chemical substance, providing an explanation or rationale for why such fate information is not relevant for the intended use of the chemical substance could inform EPA's evaluation. Frequently EPA will use QSAR models such as EPISuite™ to estimate the following parameters, measured information on the PMN or an appropriate analog are generally considered superior to QSAR models for assessment purposes. Guidelines can be found for most of the parameters below within the OECD 100 and 300 series of tests or the OPPTS 830/835 testing series.
  - Basic physical-chemical information on partitioning parameters, particularly Henry's law or air-water partitioning coefficient ( $K_{AW}$ ), soil organic carbon-water partitioning coefficient ( $K_{OC}$ ), distribution coefficient ( $K_d$ ), and octanol-water partitioning coefficient ( $K_{OW}$ ). These basic data can be useful to EPA in conducting fate modeling and estimating other fate processes.
  - Information on chemical transformation during manufacturing, processing and/or use to help identify the form of the chemical substance that is released from a given industrial process to the environment.
    - For example, the form of the chemical substance that workers are exposed to may not be the same form that downstream general population or environmental receptors are exposed to.
  - Information on degradation and bioaccumulation. All relevant environmental degradation pathways are considered including both aerobic and anaerobic biodegradation and abiotic degradation (*e.g.*, hydrolysis and photolysis).
  - Information related to behavior during waste water treatment processes and waste water treatment removal efficiencies.
    - Waste water treatment efficiency is determined by estimated rates of degradation process that occur in treatment facilities, particularly biodegradation and hydrolysis, and partitioning process, volatilization to the air and sorption to biosolids, that lead to removal of a chemical from

the wastewater. Hence, standard guideline test data on degradation and partitioning processes (e.g., laboratory, bench-scale tests) improve the determination of waste water treatment removal.

- If the waste water treatment is performed by a third party, performance and monitoring data on the water treatment facility in advance would be useful to EPA’s analysis. However, the review period does not allow for EPA to routinely search and access such data.
- Information related to incineration removal efficiency. Measured data for the chemical or an analog is preferred, but estimates without monitoring may also be informative if the basis is well described. If other ordinances (local or state) will impact incineration facilities that will receive waste this may be described in the submission.
- Information on migration through soil. Providing information on physical chemical properties (e.g., water solubility) and degradation (e.g., biodegradation) may also inform understanding of soil migration and impacts to groundwater.
- For experimental studies, provide all methodological and analytical details (full study reports are preferred) such as levels of residuals/starting materials in the chemical substance to help interpret the results of fate studies.
- Information to address the bioaccumulation potential of the chemical including *in vitro* fish metabolism studies and *in vivo* testing for fish bioconcentration factor of the chemical.
- Outputs from tools/models besides EPISuite™ may be submitted to EPA, if the tool/model is publicly available and there is a detailed rationale for how the other model is better suited for the chemical and the endpoint of concern.

### iii. Aquatic (Environmental) Hazard/Toxicity

EPA will identify endpoints/organisms of interest based on the environmental fate profile and expected environmental release pathways for a new chemical substance. If, for example, a chemical substance is expected to be present in the water column, toxicity to three organisms (*i.e.*, algae, aquatic invertebrates, and fish) will be assessed. The purpose of the Aquatic (Environmental) Hazard/Toxicity evaluation is to preliminarily characterize the following in preparation for the SAT meeting:

- Identify potential aquatic hazard concerns, using the following acute and chronic toxicity endpoint values (LC<sub>50</sub>, EC<sub>50</sub>, ChV) to identify concern levels:<sup>31</sup>

	Low Concern	Moderate Concern	High Concern
Acute	≥ 100 mg/L	1 to < 100 mg/L	< 1 mg/L
Chronic	≥ 10 mg/L	0.1 to < 10 mg/L	< 0.1 mg/L

<sup>31</sup> For more information, see: EPA (2012) 13. *Quantitative Risk Assessment Calculations*, Sustainable Futures / P2 Framework Manual, EPA-748-B12-001, at 13.2 *Performing an Aquatic Risk Assessment for SF Submissions*, available at: <https://www.epa.gov/sites/production/files/2015-05/documents/13.pdf>

- Identify the ecotoxicity hazard score (low = 1, moderate = 2, or high = 3). An ecotoxicity hazard score greater than 1 will initiate the engineering and exposure assessments.
- Derive acute and chronic concentrations of concern (“COC”) *e.g.*, acute COC for fish =  $LC_{50} \div 5$ , chronic COC for fish =  $ChV \div 10$ , where 5 and 10 are assessment factors and ChVs are chronic values that are effective concentrations at 10% (*i.e.*,  $EC_{10}$ ) extrapolated from the no observed effect concentration (“NOEC”) or the lowest observed effect concentration (“LOEC”); ChVs may also be derived from the geometric mean of the NOEC and LOEC.<sup>32</sup>
- For the overall PBT score, determine whether the new chemical substance meets the “T” criteria for aquatic organisms (*i.e.*, a chronic hazard concern level of moderate or high) (see Section III(C)(i) for a discussion of the “T” criteria for human health hazard).

When making the above determinations, EPA reviews new chemical substances in the following manner:<sup>33</sup>

- Review structure, physical-chemical properties, and structural alerts.
  - Consider molecular shape and size, fundamental physical-chemical properties (including octanol/water partition coefficients, water solubility, and melting point), presence and position of reactive functional groups, potential for absorption, charge density, minimum cross-sectional diameter of molecules, and mechanisms of toxicity.
  - Consider potential metabolites or degradates (for example, hydrolysis products).
  - Determine if chemical (or degradate) fits within a chemical category, or if the structure contains structural alerts for ecotoxicity (*e.g.*, phenols or esters).
  - Identify hazards associated with the category and/or structural alerts.
- Review submitted ecotoxicity data.
  - Identify hazards associated with or addressed by the submitted data. High quality test data on the PMN substance are generally considered to be the highest tier data for assessing ecotoxicity.
  - Determine if the data are suitable (*e.g.*, followed an established test guideline; methodological documentation allows for critical review; measured chemical concentration) for hazard and risk assessment purposes.
- If there is a Sustainable Futures submission,<sup>34</sup> or other information, such as a review by another international agency, review hazard information for data on the submitted chemical, an analog or models.

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<sup>32</sup> For more information, see: Boethling, R.S. and Nabholz, J.V. (1997) *Chapter 10 – Environmental Assessment of Polymers under the U.S. Toxic Substances Control Act*, In: *Ecological Assessment Polymers: Strategies for Product Stewardship and Regulatory Programs* (Eds. Hamilton, J.D. and Sutcliffe, R.), ISBN: 978-0-471-28782-7, John Wiley & Sons, 345 pp., at pp. 187-234.

<sup>33</sup> For more information, see: EPA (2012) *6. Estimating Aquatic Toxicity Using ECOSAR*, Sustainable Futures / P2 Framework Manual, EPA-748-B12-001, available at: <https://www.epa.gov/sites/production/files/2015-05/documents/06.pdf>

- Identify hazards associated with or addressed by the submitted data.
- Determine if the data are suitable for hazard and risk assessment purposes.
- Search for analogs using AIM<sup>35</sup>, ChemID Plus Advanced, QSAR Toolbox<sup>36</sup>, *etc.* Note that this step may be necessary even if there is submitted data, if the submitted data do not address a hazard concern based on chemical structure (*e.g.*, category or structural alert).
- Test data on the PMN substance are generally considered to be superior to QSAR values. EPA may still need to use Ecological Structure Activity Relationships (ECOSAR) Predictive Model (<https://www.epa.gov/tsca-screening-tools/ecological-structure-activity-relationships-ecosar-predictive-model>) to estimate the toxicity to the three typical ecologically relevant organisms (*i.e.*, algae, aquatic invertebrates, and fish) if the submitted ecotoxicity data does not address all three groups. ECOSAR is typically used for discrete organic chemicals.
- Since ECOSAR is primarily based on log K<sub>ow</sub>, environmental toxicity estimates could be further refined if a measured log K<sub>ow</sub> value is provided in the notification. In the absence of a measured log K<sub>ow</sub> value, EPA may use the log K<sub>ow</sub> value estimated using EPISuite™.
- As a general rule, EPA will consider that an organic new chemical substance has a low hazard if the log K<sub>ow</sub> is greater than 8.
- Measured water solubility values assist with informing the ecological hazard characterization. In the absence of measured water solubility data, EPA may use the water solubility value estimated using EPISuite™.
- EPA may consider environmental aquatic hazard to be low for a specific toxicity endpoint value (96-h fish LC<sub>50</sub>), if that value is greater than ten times the measured water solubility value or the measured water solubility value is less than 1 microgram/liter (< 1 part per billion).
- Derive the COC, for the new chemical substance, by dividing the lowest acute and/or chronic toxicity value by an assessment factor (taking into account lab-to-field/inter-species variability).
- COCs are then used in conjunction with the exposure assessment, that is, compared with estimated surface water concentrations, as discussed in Section V to estimate potential risks.

*EPA recommends submitters consider the following information on the new chemical substance:*

- EPA will consider the following types of information about the chemical substance during the New Chemical Review Process. If the submitter believes that any or all of this

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<sup>34</sup> For more information, see: EPA (2012) 14. *Completing a Sustainable Futures PMN Submission*, Sustainable Futures / P2 Framework Manual, EPA-748-B12-001, available at: <https://www.epa.gov/sites/production/files/2015-05/documents/14.pdf>

<sup>35</sup> Information on analog identification is available here: EPA (2012) 9. *Analog Identification Methodology (AIM)*, Sustainable Futures / P2 Framework Manual, EPA-748-B12-001, <https://www.epa.gov/sites/production/files/2015-05/documents/09.pdf>

<sup>36</sup> The OECD QSAR Toolbox is publicly available software, that is available for download at the following: <http://www.oecd.org/chemicalsafety/risk-assessment/oecd-qsar-toolbox.htm>

information is not applicable or relevant to the new chemical substance, providing an explanation or rationale for why such ecotoxicity information is not relevant for the intended use of the chemical substance could inform EPA's evaluation.

- Information related to environmental hazards for both short-term (acute) and long-term (chronic) exposures.
- If chemical substances are “difficult-to-test”, submitters should consider engaging in a pre-notice communication with EPA prior to toxicity test initiation.
- Information on % amine-nitrogen content for all relevant chemical substances (e.g., polycationic polymers).<sup>37</sup>
- Submitters should consider whether there are acceptable analog(s) for any toxicity endpoint to support the New Chemical Review process. Analog data may be useful to provide multiple lines of scientific evidence for determination of hazard concerns, even if data are available for the chemical substance.
  - Provide justification for consideration of the analog for the endpoint(s) identified.
  - Provide chemical name and CAS numbers of all analogs.
  - Provide clear structural representation of the analog substance(s). It is best to provide a visual representation of the molecular structure along with that of the chemical substance. If EPA cannot determine the molecular structure or composition of the analog, it will not be considered.
  - Provide full studies on the analogs to better ensure consideration by EPA.

### ***E. Environmental Releases/Exposure Assessments***

If, at SAT, it is determined that exposure and release profiles are needed for the new chemical substance, chemical engineers and exposure assessors develop the identified types of exposure and release profiles, which may include the following:

- Engineering assessment.
  - Process information and worker exposures.
  - Environmental release and disposal.
- General population exposures.
- Consumer exposures.
- Environmental exposure to non-human receptors.

#### **i. Engineering Assessment**

The engineering assessments begin with EPA importing physical-chemical property information into the modeling software, ChemSTEER.<sup>38</sup> This information is determined from earlier steps in the New Chemical Review process. The ChemSTEER model is, basically, a mass

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<sup>37</sup> For more information, see: Boethling, R.S. and Nabholz, J.V. (1997) *supra* note 327.

<sup>38</sup> The Chemical Screening Tool for Exposures and Environmental Releases (ChemSTEER) is publicly available software, that is available for download at the following: <https://www.epa.gov/tsca-screening-tools/chemsteer-chemical-screening-tool-exposures-and-environmental-releases>



balance/material flow model and only requires PV and four basic physical-chemical properties (*i.e.*, vapor pressure, molecular weight, density, and water solubility).<sup>39,40</sup> The notification and supporting attachments from EPA Form 7710-25 (Rev. 5-95) are examined for additional information to use in order to create the occupational exposure and environmental release assessment based on how the new chemical substance is managed from its creation (manufacturing), until it is no longer available for release or exposure in the occupational setting (use). The information from the notification is used to refine the output from ChemSTEER, as discussed below.

EPA assesses each industrial/commercial step in the new chemical substance's domestic life cycle. These steps typically include manufacturing, processing, and end use of the chemical. For each life cycle step, the number of sites, facility-level throughputs (kg chemical/site-day), and days of operation are estimated based on available information in the notification and a mass balance. EPA then presents a description of process flow and identifies potential occupational exposure activities and environmental release sources, such as container loading/unloading, equipment cleaning, *etc.* Next, EPA estimates dermal and inhalation occupational exposures in mg/day, including frequency, duration, and number of workers exposed, as well as environmental releases to all media (*e.g.*, water, incineration, landfill, air, and underground injection) in kg/site-day including the release frequency (days/year).

Where relevant data are not included in the notification, EPA will derive estimates using various sources including: exposure and release models within ChemSTEER using default, conservative assumptions;<sup>41</sup> OECD Emission Scenario Documents;<sup>42</sup> and EPA Generic Scenarios<sup>43</sup> which describe industrial practices relevant to the case at hand. Information from previous notifications and assessments may also be used. Generally, in the absence of chemical- or facility-specific data provided in a notification, EPA uses estimates that are intended to be protective of human health and the environment.

*EPA recommends submitters consider the following information on the new chemical substance:*

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<sup>39</sup> See, *e.g.*, EPA (2012) *11. Estimating Workplace Exposure and Industrial Releases Using ChemSTEER*, Sustainable Futures / P2 Framework Manual, EPA-748-B12-001, at p. 11-2, available at: <https://www.epa.gov/sites/production/files/2015-05/documents/11.pdf>

<sup>40</sup> For more information, see: EPA (2012) *Appendix G. ChemSTEER Case Study*, Sustainable Futures / P2 Framework Manual, EPA-748-B12-001, at pp. G2 and G3, available at: <https://www.epa.gov/sites/production/files/2015-05/documents/appendg.pdf>

<sup>41</sup> For more information, see: EPA (2013) *ChemSTEER User Guide – Chemical Screening Tool for Exposures and Environmental Releases*, U.S. Environmental Protection Agency, 399 pp., at pp. 253-261 (Quick Summary of ChemSTEER Inhalation Exposure Models), pp. 263-265 (Quick Summary of ChemSTEER Dermal Exposure Models), and pp. 148-155 (Quick Summary of ChemSTEER Release Models).

<sup>42</sup> OECD Emission Scenario Documents are available at the following: <http://www.oecd.org/chemicalsafety/risk-assessment/emissionsceniordocuments.htm>

<sup>43</sup> EPA Generic Scenarios are available at the following: <https://www.epa.gov/tsca-screening-tools/using-predictive-methods-assess-exposure-and-fate-under-tsca#fate>

## 1. *Process Information and Worker Exposures*

EPA will use generally conservative assumptions when assessing the potential risk(s) the new chemical substance may pose to workers; therefore, submitters should consider whether the following types of information are relevant to their new chemical substance(s).

- The expected worker exposures for each worker activity of the manufacturing/processing/use operations, including information on:
  - What specifically the worker is doing and what physical state and concentration of chemical substance (*e.g.*, unloading slurry of 40% new chemical substance in organic solvent from a 55-gallon drums).
  - If exposure is not expected for a specific activity, EPA would update the default assumptions if a specific explanation and rationale is available (*e.g.*, quick connect fittings and manifold are purged prior to disconnect and supporting schematic of the quick connect equipment is included).
- For manufacturing, the estimated mass balance related information (including throughput rate, number of days of production, and number of batches per day for the batch or continuous operation) for the maximum 12-month PV (for first three years of production).
  - Submitters should consider avoiding gross overestimates of PV values, as this can result in erroneously high estimates for release and exposure values.
- The percent of the new chemical substance in the formulation for each category of manufacturing, processing, and use. This information is one of the five possible input values used in the specific mass balance parameters within ChemSTEER.<sup>44</sup> For example, for a coating use, provide the maximum weight percent of the new chemical substance in the final coating formulation; if different formulations are anticipated, provide the maximum weight percent *for each*. The concentration of the new chemical substance is used in estimating exposure dose in which the highest concentration is used, so it is beneficial to be precise and not over estimate.
- If the new chemical substance is submitted as a Low Volume Exemption and PV is not marked “binding” in EPA Form 7710-25 (Rev. 5-95), provide scale-up batch parameters (*e.g.*, kg per batch or day, hours per batch or day, batch or operation days per year) for a PV of 10,000 kg/yr. See: <https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/low-volume-exemption-new-chemical>. In cases where the binding option is not marked, EPA assesses releases and exposures assuming the PV could be as high as 10,000 kg/yr.
- Dermal exposure data for the new chemical substance or for a structurally similar chemical used in a similar setting. In the absence of data, dermal exposures are estimated using dermal exposure models in ChemSTEER.<sup>45</sup>

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<sup>44</sup> *Id.* at p. 11-7; see also: EPA (2012) *supra* note 33 at p. G-3.

<sup>45</sup> For more information, see: EPA (2013) *ChemSTEER User Guide – Chemical Screening Tool for Exposures and Environmental Releases*, U.S. Environmental Protection Agency, 399 pp., at pp. 263-265 (Quick Summary of ChemSTEER Dermal Exposure Models).

- Identification of any operations or activities that are conducted under non-standard temperatures or pressures. Activities occurring at elevated temperatures may cause potential inhalation exposures to workers. Conversely, activities occurring at reduced temperatures may lower volatility and the corresponding inhalation exposures.
- The specific type of personal protective equipment (“PPE”) that will be used at the manufacturing site and, to the extent known, at processing and use sites.
  - Information on type of gloves used (*e.g.*, material composition, penetration time of glove material, glove thickness, name/model number). This information will support EPA’s determination whether “impervious gloves” are used. Specific information of the kind of protective clothing (*e.g.*, goggles, facemasks, suits, *etc.*, including specific brand names/model numbers) is also useful for refining the assessment.
  - Information on type of respirator used (*e.g.*, name/model number, cartridge type, breakthrough time *for the new chemical substance* or a close analog with similar properties, assigned protection factors (“APF”), and maximum use concentrations).
  - PPE is generally considered during risk management (at focus and during post-focus). The engineering report is performed with the assumption of no PPE and then if risks are identified, the submitter’s information on PPE (including the specific APF) is taken into consideration as to whether that risk has been mitigated.
- If the new chemical substance is manufactured, processed, or used as a solid or powder:
  - Indicate whether the manufacture, processing, and/or use of the new chemical substance is expected to result in suspended particles (also referred to as dust) in air thereby creating a potential inhalation exposure. If so, EPA would consider supporting measured data on particle size distribution and/or type of solid material (*e.g.*, powder, wet cake with 30% moisture content, paste, or slurry).
    - In the absence of particle size distribution data, EPA may assume there are potential inhalation exposures to the new chemical substance.
  - Provide description and efficiency information (with supporting data) for air pollution control technologies/systems used (*e.g.*, bag filter, dust collector, local exhaust ventilation) and how the technologies/systems would reduce releases and/or worker exposures.
  - Specify the type and size of container transporting the solid new chemical substance for each operation.
  - Indicate in what form the new chemical substance will be distributed to processors and users (*e.g.*, solid, liquid, or paste form).
- Inhalation exposure data (personal and/or area monitoring data) for the new chemical substance or structurally similar chemical used in a similar setting. In the absence of data, EPA may assume a mass concentration limit of particulate in air of up to 5 mg/m<sup>3</sup> (respirable) or 15 mg/m<sup>3</sup> (total particulates) per the OSHA Particulates Not Otherwise Regulated (PNOR) PEL-Limiting Models.<sup>46</sup>

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<sup>46</sup> For more information, see: EPA (2013) *ChemSTEER User Guide – Chemical Screening Tool for Exposures and Environmental Releases*, U.S. Environmental Protection Agency, 399 pp., at pp. 253-261 (Quick Summary of ChemSTEER Inhalation Exposure Models).

- Include the Safety Data Sheet (“SDS”) or Materials Safety Data Sheet (“MSDS”). Formerly referred to as MSDS, SDSs are developed by the manufacturer and provided by the product supplier to the user.

## 2. *Environmental Release and Disposal Information*

EPA often sees submissions that lack specificity with regard to the following types of information on the new chemical substance. In the absence of this type of information, EPA will use generally conservative assumptions when assessing the potential risk(s) the new chemical substance may pose from environmental releases resulted from manufacturing, processing, use and disposal.

- All possible environmental releases of the new chemical substance for the specified operation type or equipment. EPA typically expects releases during unloading/loading, container cleaning, and equipment cleaning.<sup>47,48</sup> EPA will consider the following types of information during new chemical assessment:
  - Unit operation (*e.g.*, filter, reactor) or equipment (*e.g.*, process vessel) and capacity or throughput/batch related information (*e.g.*, quantity of batch, # of batches)
    - Description of unit operations and equipment including schematic drawing of the equipment (*e.g.*, reactor or vessel schematic drawing). Provide a narrative how the unit operation or equipment is cleaned (*e.g.*, by pumping solvent into vessel to clean residual remaining in vessel and then removing rinsate (containing PMN substance) out of vessel via pumping or by draining through an orifice or valve from the vessel. Provide supporting information *e.g.* drawing showing location of orifice or valve and location and elevation of vessel. For equipment cleaning, in the absence of specific information about equipment configuration (with supporting schematic drawing), EPA may assume up to 2% of residual from cleanup activity (based on daily throughput or batch) for a multiple-vessel operation.
  - Amount of the new chemical substance released (in kg) per day or per batch and supporting information (*e.g.*, release data from an analogous chemical used in similar process)
  - Media of release (*e.g.*, stack air, fugitive air, surface water, on-site or off-site land or incineration, industrial wastewater treatment facility [“WWTF”], publicly owned treatment works [“POTW”], or other control technology that will be used to limit the release of the PMN to the environment).
  - Control technology efficiency (*e.g.*, the incineration efficiency for a similar product formulation containing a similar chemical to the chemical substance is between 99.1-99.5%; be sure to provide the supporting information). EPA may consider the amount of documentation available for supporting a suggested efficiency before implementing it in the assessment.

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<sup>47</sup> For more information, see: EPA (2012) *11. Estimating Workplace Exposure and Industrial Releases Using ChemSTEER*, Sustainable Futures / P2 Framework Manual, EPA-748-B12-001, at p. 11-5, available at: <https://www.epa.gov/sites/production/files/2015-05/documents/11.pdf>

<sup>48</sup> *Id.*

- The frequency of equipment cleaning (*e.g.*, every day, after every batch, once a year)
- The substance that is used to clean the equipment and its physical state (*e.g.*, water, solvent, steam)
- For all releases, provide estimates of the amount and the frequency of releases. EPA needs detailed information on the basis for each estimate in order for the estimate to be considered by the Agency.
- Description of the unit transport container type, capacity and container cleaning procedure and frequency including, for example, the following information:
  - Five 5,000-gallon trucks used to store/transport the chemical substance are dedicated and only rinsed once every 20 deliveries.
  - The rinsate that contains the chemical substance is put down the drain, incinerated, *etc.*
  - The cleaning and disposal of the transport containers are performed by the submitter on site. If the containers are cleaned or disposed of off-site, provide available information including the cleaning methods, frequency of cleaning, and estimated amount of new chemical substance released per cleaning.
  - The information above is then used with release estimation models within ChemSTEER to estimate releases from residuals remaining in different container sizes.<sup>49</sup> In the absence of specific information, EPA generally assumes that the new chemical substance is transported in 55-gallon drums, and the remaining heel (*i.e.*, drum residual) would be 3% loss fraction to water.
- Detailed description of disposal practices (*e.g.*, surface impoundment, landfill and type of landfill) for the new chemical substance at manufacturing, processing, and use sites for those controlled by the submitter and, if known, at sites not controlled by the submitter.
- The National Pollution Discharge Elimination System (“NPDES”) permit numbers (*i.e.*, non-storm water permit numbers) for WWTFs at a manufacturing site(s), a known processing site(s), and a known use site(s), or the NPDES permit numbers for the POTWs receiving wastewater from the facility(ies).
  - Specify the type of wastewater treatment technologies used at the facility(ies).
  - Provide any removal efficiency information for onsite treatment unit operations. Indicate whether the information estimated or measured.
- The Clean Air Act operating permit numbers for facilities with expected releases to air.
  - Specify the type of air pollution control technologies used at the facility(ies).
  - Provide any removal efficiency information for onsite treatment unit operations. Indicate whether the information is estimated or measured and provide supporting information.
  - Is the facility under a Leak Detection and Repair program (related to the monitoring and management of fugitive releases)? If “yes,” describe the program.

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<sup>49</sup> For more information, see: EPA (2013) *ChemSTEER User Guide – Chemical Screening Tool for Exposures and Environmental Releases*, U.S. Environmental Protection Agency, 399 pp., at pp. 148-155 (Quick Summary of ChemSTEER Release Models).

## ii. Non-Occupational General Population, Consumer and Environmental Exposures

When conducting a review of new chemical substances, non-occupational and environmental exposure assessments are generally performed if there are hazard concerns for the general population, consumers, or environmental receptors. Regardless of identified hazard concerns, such exposures are also assessed if the PV of the new chemical substance is greater than or equal to 100,000 kg/year (*i.e.*, exposure-based trigger), or if the new chemical substance is identified as P2B2 per the environmental fate evaluation conducted for the SAT meeting.

Non-occupational, general population exposures include any types of exposure that occur outside the boundaries of the workplace, except for use of consumer products. Exposure to the general population may occur as a result of releases to the environment (*i.e.*, air, surface water, landfills) from manufacturing, processing, and industrial or commercial uses of a new chemical substance. The associated routes of exposure to the general population include inhalation of ambient air (*i.e.*, air outside the boundaries of the workplace), ingestion of drinking water or fish contaminated by the new chemical substance. Use of monitoring data reflecting actual concentrations of a chemical substance in various environmental media is the preferred approach to examine potential exposures; however, such data are rarely available for new chemical substances. As such, modeling methods are employed in the absence of reliable monitoring data to estimate exposures using the General Population and Ecological Exposure from Industrial Releases Module embedded within the Exposure and Fate Assessment Screening Tool (E-FAST).<sup>50</sup>

Consumer exposures are distinct from general population exposures that may result from releases to the environment from industrial or commercial activities. Consumer exposures may occur through the use of household products through dermal contact with consumer products and/or inhalation of the new chemical substance that volatilizes from consumer products or is released from aerosol products in indoor air. Such exposures are generally estimated using the Consumer Exposure Module (CEM) embedded within E-FAST. The use of consumer products that are added to water during use, *e.g.*, laundry detergents, if applicable, can be assessed using the Down-the-Drain Module embedded within E-FAST.

Environmental exposures resulting from releases to water, either from sites involved in the manufacture, processing, or use of the new chemical substance or from certain consumer uses, as noted above, are reflected by the Predicted Environmental Concentration (PEC) in surface water, which is also estimated using E-FAST. For more information on how to use E-FAST or its embedded models, please see the E-FAST Documentation Manual<sup>51</sup> or EPA's Sustainable

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<sup>50</sup> E-FAST is publicly available software, that is available for download at the following: <https://www.epa.gov/tsca-screening-tools/download-and-install-instructions-e-fast-exposure-and-fate-assessment-screening>

<sup>51</sup> EPA (2007) *Exposure and Fate Assessment Screening Tool (E-FAST), Version 2.0, Documentation Manual*, available at: <https://www.epa.gov/sites/production/files/2015-04/documents/efast2man.pdf>

Futures/P2 Framework Manual,<sup>52</sup> which contains a chapter dedicated to estimating general population and aquatic exposure using E-FAST.

The general population, consumer, and/or environmental exposure assessment process begins with a review of relevant information contained in the engineering report including the following: consumer use status and weight fraction, if applicable; PV; site-specific information that may inform use of a site-specific NPDES code; media of predicted releases (*e.g.*, water, air, incineration, landfill); number of sites associated with predicted releases; and process description, which may be used to inform Standard Industrial Classification (SIC) code selection and/or consumer exposure scenario and weight fraction. Additional input parameters are gathered from the evaluations on human health hazard/toxicity, environmental fate, and aquatic (environmental) hazard/toxicity. The relevant environmental fate inputs include: fish BCF or BAF value, wastewater treatment (WWT) removal efficiency, persistence and bioaccumulation ratings (*i.e.*, P and B scores), and soil migration. The primary hazard/toxicity inputs include the routes of concern for human exposure (*i.e.*, ingestion, dermal, and/or inhalation) and the chronic COC for aquatic species exposure. Collectively, this information reflects the necessary inputs into E-FAST and CEM. As noted, some consumer uses may also be assessed for releases to water during use and subsequent human and environmental exposures.

Most of the described input parameters are determined during the preceding evaluations on human health/toxicity, environmental fate, and aquatic (environmental) hazard/toxicity. In the absence of submitted data, such inputs may be based on analog, conservative assumptions, or model estimates. Below is a list of the key exposure modeling input parameters and a brief description of how they are used in exposure assessment:

- **SIC Code:** Each generic SIC code programmed into E-FAST is associated with a stream flow distribution, which is applied to water releases when estimating the PEC(s). Use of an SIC code generally results in a more conservative estimate of stream concentration when compared with use of a site-specific NPDES code.
- **NPDES Code:** Each site-specific NPDES code is associated with a stream flow, which is applied to water releases when estimating the PEC(s). In the absence of a site-specific NPDES code, EPA may instead use a stream flow associated with a more generic SIC code.
- **WWT Removal Efficiency (%):** This input is determined during the environmental fate evaluation and is applied to water release inputs in E-FAST, thereby reducing the magnitude of water releases.
- **Chronic COC:** This input is determined during the aquatic (environmental) hazard/toxicity evaluation and is compared to the chronic PEC calculated by E-FAST (*i.e.*, the PEC resulting from any water releases occurring over 20 days or more).

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<sup>52</sup> EPA (2012) 12. *Estimating General Population and Aquatic Exposure using E-FAST*, Sustainable Futures / P2 Framework Manual 2012 EPA-748-B12-001, 26 pp., available at: <https://www.epa.gov/sites/production/files/2015-05/documents/12.pdf>

- **Production Volume (kg/year):** This input is provided by the submitter. A production volume equal to or greater than 100,000 kg/year will be run as an exposure based case and total releases and dose estimates will be compared against exposure-based criteria<sup>53</sup>.
- **Incineration Destruction and Removal Efficiency DRE (%):** DRE is applied to predicted releases from incineration releases.
- **Fish BCF or BAF:** This input is determined during the environmental fate evaluation and is applied to the predicted environmental concentration (PEC) to estimate a fish concentration that is then used to estimate general population exposures from fish ingestion.
- **PB rating (1, 2, 3):** This input is determined during the environmental fate evaluation. If a new chemical substance is considered persistent and bioaccumulative, total releases and dose estimates will be compared against persistent and bioaccumulative criteria<sup>54</sup>.
- **Migration Rate (negligible, slow, moderate, rapid):** This input is determined during the environmental fate evaluation and is applied to the estimation of general population oral exposure to landfill releases, when non-negligible leaching to groundwater is predicted.
- **Consumer Product Weight Fraction (%):** This input is one of the major chemical-specific inputs into CEM.

The described input parameters and population exposure factors (*e.g.*, inhalation rate, body weight, drinking water intake) are employed by E-FAST or CEM to generate the following key exposure outputs: acute dose rate (ADR in mg/kg-bw/day); lifetime average daily dose (LADD in mg/kg-bw/day); PEC ( $\mu\text{g/L}$ ) in surface water, reflected by the 7Q10 stream concentration (*i.e.*, the concentration estimated using the 7Q10 flow – the 7 consecutive days of lowest flow over a 10-year period); and the number of days per year a chronic COC has been exceeded in surface water. The population exposure factors are sourced from the 2011 Exposure Factors Handbook<sup>55</sup> and are pre-populated in E-FAST and CEM for several life stages: adult; youth (16-20 years); youth (11-15 years); child (6-10 years); small child (3-5 years); infant (1-2 years); and infant (<1 year).

EPA will generally use conservative assumptions when assessing the potential risks that the new chemical substance may pose from exposures to the general population, consumers, and/or the environment; therefore, submitters should consider whether the following types of information are relevant to their new chemical substance(s).

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<sup>53</sup> Exposure based exceedance criteria for general population and ecological exposure modeling: Human potential dose estimates  $\geq 3.0\text{E-}03$  mg/kg-bw/day; total post-treatment release to all media  $\geq 10,000$  kg/year; or total post-treatment release to surface water  $\geq 2,000$  kg/year.

<sup>54</sup> Persistent and Bioaccumulative exceedance criteria for general population and ecological exposure modeling: Human potential dose estimates  $\geq 3.0\text{E-}03$  mg/kg-bw/day; total post-treatment release to all media  $\geq 2,000$  kg/year; or total post-treatment release to surface water  $\geq 200$  kg/year.

<sup>55</sup> EPA (2011) *Exposure Factors Handbook: 2011 Edition*, National Center for Environmental Assessment, Office of Research and Development, U.S. Environmental Protection Agency, Washington, D.C., EPA/600/R-090/052F, available at: [http://ofmpub.epa.gov/eims/eimscomm.getfile?p\\_download\\_id=522996](http://ofmpub.epa.gov/eims/eimscomm.getfile?p_download_id=522996)



### **1. General Population Exposure**

- Characterize the magnitude and distribution of direct-release scenarios. Characterization of exposed populations surrounding the manufacturing, processing, or use facilities. Provide the distance to the nearest residence. EPA generally assumes a distance of 100 meters to the nearest residence for general population exposure to incineration or fugitive releases.
- The degree to which a new chemical substance may be removed in POTWs and/or through on-site treatment at a WWTF before release to the environment. Removal efficiency has the potential to significantly impact the resulting exposures to the downstream general population and ecological receptors. In the absence of specific information, EPA will use a conservative removal efficiency based on the EPISuite™ sewage treatment plant (STP) model (typically 90%).
- Information on the potential for the new chemical substance to migrate to groundwater under any conditions where the chemical substance is released to the environment.

### **2. New Chemical Substances in Products Used by Consumers**

- Information characterizing the properties of the product such as density, physical form, method of application (*e.g.*, spray, brush, and/or roll-on), and whether and how much dilution occurs during routine use.
- Description and rationale for the expected typical setting for use (*e.g.*, outdoors, indoors, residential, and/or commercial).
- Estimate of the frequency of use (*e.g.*, daily, weekly, and number of times per year)
- Estimate and rationale for the duration of use (*e.g.*, the product is used for minutes or hours).
- Describe the consumption rate for any single use (*e.g.*, the volume or weight consumed during each use) and explain the basis for that consumption rate.
- Estimate of the number and types of individuals (receptors) who may use the new chemical substance or product containing the new chemical substance.
  - Examples: high-frequency consumer use (*e.g.*, product frequently used by individual), low-frequency consumer use, estimated extent of consumer use (*e.g.*, size of consumer market, estimated number of users), use by children, *etc.*
- Information on the circumstances of use that may influence exposure such as expected temperatures during use, whether products are manipulated, cut, abraded, or sprayed.
- Information on the circumstance under which the consumer would use the product containing the new chemical substance that may influence exposure in ways not typically considered such as variable on-site application, chemical reaction or degradation during use, potential for abrasion, manipulation, or other physical degradation during use, or other potential for elevated exposures during the range of expected circumstances of the typical use.

### **3. Articles**

- Any information or product testing data on the emission or migration of new chemical substances from products or articles (or the types of materials they are envisioned to be made of, *e.g.*, plastic) into environmental media. For examples of types of exposure testing data relevant to the New Chemical Review process, see: EPA Indoor Exposure

Product Testing Protocols. Note: version 2.0 is currently available (2017);<sup>56</sup> an updated version is expected soon.

## IV. RISK CALCULATIONS

### A. Human Health Risk Assessment

If a point of departure (POD) is identified during the human health hazard/toxicity data review, then risks are quantified. To evaluate and quantify whether potential risks exist in the New Chemical Review process, EPA generally uses the Margin of Exposure approach (MOEs). The calculated MOEs are derived by dividing the POD by the exposure estimates generated from the engineering and exposure assessments. The MOEs are then compared to a benchmark MOE to determine if potential risks of concern are present. Potential risks are identified if the calculated MOE is below the benchmark MOE.

The benchmark MOE is obtained by multiplying the total uncertainty factors (UFs) associated with each POD. These UFs typically include: (1) the variation in susceptibility among members of the human population (*i.e.*, inter-individual or intraspecies variability or  $UF_H$  = default of 10), and (2) the uncertainty in extrapolating animal data to humans (*i.e.*, interspecies uncertainty or  $UF_A$  = default of 10). The default  $UF_A$  consists of a factor of 3.16 for toxicokinetics (TK) and 3.16 for toxicodynamics (TD) (*i.e.*,  $UF_A = TK \times TD =$  default of 10); however, the TK factor may be modified, typically to 1, when a human equivalence dose (HED) or human equivalence concentration (HEC) is calculated to derive the POD (*i.e.*,  $UF_A = 1$  for  $TK \times 3$  for  $TD = 3$ ). An additional UF may be added if the POD is based on a LOAEL, rather than a NOAEL (*i.e.*, LOAEL-to-NOAEL extrapolation or  $UF_L = 10$ ). Hence, in the New Chemical Review process, benchmark MOEs are typically 100 or 1000; however, when specific data are available to justify changes, they may be adjusted downward or upward.

If a POD is not available, a qualitative risk finding may be made. For example, if test data on a new chemical substance indicates it elicited dermal sensitization, EPA generally identifies the new chemical substance as a potential respiratory sensitizer as well; however, it is generally not possible to identify a POD for respiratory sensitization. Therefore, if there are potential inhalation exposures to workers from a suspected respiratory sensitizer, EPA may qualitatively identify respiratory sensitization as a potential risk for workers. In some cases, hazards are identified based on a structural alert (*e.g.*, acrylamides and carcinogenicity), but data are not available to derive a quantitative POD (a benchmark MOE cannot be quantified). In such a case, if there are populations that may be exposed, EPA may qualitatively identify carcinogenicity as a potential risk, based on the qualitative assessment of hazard and estimated exposures.

In some cases, EPA has estimated exposures for a new chemical substance, under the conditions of use; however, there was no hazard information available on the new chemical substance, including no structural alerts or acceptable analogs with test data. Under these circumstances,

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<sup>56</sup> EPA (2017) *Indoor Exposure Product Testing Protocol, Version 2.0*, Office of Chemical Safety and Pollution Prevention, U.S. Environmental Protection Agency, EPA document number: 740-S1-7002, 104 pp., available at: [https://www.epa.gov/sites/production/files/2018-01/documents/indoor\\_exposure\\_testing\\_protocols\\_version\\_2.pdf](https://www.epa.gov/sites/production/files/2018-01/documents/indoor_exposure_testing_protocols_version_2.pdf)

EPA cannot perform a reasoned evaluation of potential risks and will generally request testing on the new chemical substance.

If potential risks are identified, EPA may refine the risk calculations based on absorption or, if relevant, consideration of the weight percentage of the new chemical substance that the structural alert or component of concern comprises. For example, if the structural component of a polymer is associated with a hazard concern for a particular chemical type, then EPA will generally adjust the estimated exposures based on the weight percent of the particular chemical type and will modify the risk calculations accordingly.

Risk characterization is part of the risk assessment and takes the form of a conclusion about the chemical substance's potential for health and environmental risk. It embodies the effects of potential concern, the route and magnitude of expected exposure, and numbers in the population estimated to be exposed.

### ***B. Aquatic (Environmental) Risk Assessment***

EPA evaluates potential acute and chronic risks of concern to aquatic organisms by comparing potential environmental concentrations (PEC) to acute and chronic COCs. The PEC information is provided in the exposure assessment generated using E-FAST.

#### **i. Evaluation of Acute Aquatic Risk**

EPA compares acute COCs directly to the PEC. A potential for risks exists if the PEC is greater than the acute COC. For example, if the lowest acute COC value for the three target species (*i.e.*, fish, daphnia, and green algae) is 20 parts per billion (ppb) for algae and the E-FAST General Population and Ecological Exposure module results show a PEC (or 7Q10 surface water concentration) of 45 ppb, then there is a potential risk for acute exposures.

#### **ii. Evaluation of Chronic Aquatic Risk**

If the PEC is greater than the chronic COC, then potential chronic risks may exist. Chronic aquatic risk is further evaluated by determining the number of days per year the chronic COC is exceeded. If the chronic COC is exceeded by the PEC for less than 20 days per year as estimated by E-FAST's probabilistic dilution model (PDM), then no potential chronic risks are identified for the environment. If the chronic COC is exceeded more than 20 days per year, then a potential chronic risk of concern is identified.<sup>57</sup>

#### **iii. Evaluation of Soil or Sediment Risk**

Potential acute and chronic risks to soil and/or sediment-dwelling organisms are assessed by EPA when physical-chemical and fate properties indicate that the new chemical substance will partition into soils or sediments, and there are acute and/or chronic aquatic risks. Use and exposure information are also considered when EPA evaluates soil and sediment exposure

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<sup>57</sup> The 20-day criterion is derived from partial life cycle tests (*e.g.*, daphnid chronic and fish early life stage tests) that typically range from 21 to 28 days in duration. It is important to note that the PDM model estimates only the total number of days out of 1 year that the COC is exceeded. The days are not necessarily consecutive, and thus the 20-day criterion is a conservative one.

pathways. For example, if a new chemical substance has a low water solubility, a high log  $K_{ow}$ , a high log  $K_{oc}$ , a production volume of 5,000,000 kg/yr, EPA will generally recommend soil and/or sediment toxicity testing.

## **V. FOCUS MEETING AND REGULATORY DECISIONS**

Next in the New Chemical Review process, an interdisciplinary team of chemists, biologists, toxicologists, engineers, fate assessors, and exposure assessors finalize their respective sections of the risk assessment in preparation for the Focus Meeting. At the Focus Meeting, the interdisciplinary team discusses the results of the risk assessment and effects of potential risk mitigation options (*e.g.*, how to limit potential releases or exposure pathways) with risk managers. Preliminary risk management recommendations made at the Focus Meeting or subsequent decision meetings with managers or decisions that further analysis is needed are informed by the results of the risk assessment and may consider chemical categories, exposure-based reviews, and exemption criteria as they pertain to limiting risks.

## **VI. STANDARD REVIEW**

An outcome of the Focus Meeting may be to put the new chemical substance into “Standard Review”. A typical scenario leading to a Standard Review is when the screening evaluation conducted prior to the FOCUS meeting results in identification of significant risks or studies were submitted with the notification that need a more thorough review. During the Standard Review, EPA will perform a more in-depth evaluation of the new chemical substance, typically based on any newly available information provided by the submitter after the initial notification was submitted.

## VII. POST-SUBMISSION COMMUNICATION

If risks are identified in the risk assessment, a program manager (risk manager) typically works with the submitter to identify additional information that would assist EPA in developing strategies to mitigate the risks. Effective communication between the program manager and submitter is essential to this interaction.

### **i. Communication Recommendations**

- It is good practice to inform your EPA Program Manager (e-mail or phone message) that you have electronically submitted an amendment or document *via* CDX or that you have sent a document *via* fax.
- When a suspension of more than 15 days appears to be needed, we encourage you to submit a written request for suspension thru CDX for the longer time period.
- Become familiar with the TSCA Section 5(e) Consent Order boilerplate on EPA's website (<https://www.epa.gov/reviewing-new-chemicals-under-toxic-substances-control-act-tsca/new-chemicals-program-boilerplates>).
- Consider using the "binding option" in EPA Form 7710-25 (Rev. 5-95). Indicating a willingness to be bound to certain information (see sub-bullets below) in the notification does not by itself prohibit the submitter from deviating after the end of the review from the information (except chemical identity) which had been reported in EPA Form 7710-25 (Rev. 5-95) (unless the submitter and the Agency enter into a binding TSCA § 5(e) Consent Order), but it does provide the starting point for discussions between EPA and the submitter.
  - Pollution control technology and efficiency
  - Physical form(s) of the new chemical substance
  - Worker protection/engineering controls
  - Process description
  - Use information

## **ii. Additional Information and Training**

The Sustainable Futures program provides the public with educational training workshops on the New Chemical Review process and use of EPA's computerized models and tools. The EPA's website on the Sustainable Futures training can be found at: <https://www.epa.gov/sustainable-futures/sustainable-futures-training-workshops>.

The program also encourages chemical developers to use EPA's models and methods to screen chemical substances for potential risks early in the development process or before submission of a chemical substance notification. Prescreening chemicals for hazard concerns helps companies anticipate, and gives them the information and opportunity to avoid, developing chemicals of concern. Sustainable Futures training workshops are open to the public, and EPA encourages companies to host a Sustainable Futures workshop. This website provides all materials for training and can be used in conjunction with a predefined two and one-half day agenda that covers training on each of the models and methods that EPA uses.