



Environmental Defense Fund

Comments on

Draft Scope of the Manufacturer-Requested Risk Evaluation to Be Conducted for Octamethylcyclotetra-siloxane (Cyclotetrasiloxane, 2,2,4,4,6,6,8,8-octamethyl-)

(D4)

(CAS No.: 556-67-2)

Under the Toxic Substances Control Act

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Introduction and Summary

Environmental Defense Fund (EDF) appreciates the opportunity to comment on the Draft Scope of the manufacturer-requested Risk Evaluation for Octamethylcyclotetra-siloxane (Cyclotetrasiloxane, 2,2,4,4,6,6,8,8-octamethyl-) (D4) (Draft D4 Scope).¹ EPA received, and granted, a request to conduct a Toxic Substance Control Act (TSCA) risk evaluation of D4 from the Silicones Environmental, Health and Safety Center (SEHSC), on behalf of Dow Silicones Corporation, Elkem Silicones USA Corporation, Evonik Corporation, Momentive Performance Materials, Shin-Etsu Silicones of America, Inc., and Wacker Chemical Corporation.² EPA must adhere to the same risk evaluation requirements under TSCA for high priority chemicals when conducting manufacturer-requested risk evaluations, including consideration of all “reasonably available” information and use of the “best available science.” The Administrator is not

¹ U.S. EPA. (2021, August). *Draft Scope of the Risk Evaluation for Octamethylcyclotetra-siloxane (Cyclotetrasiloxane, 2,2,4,4,6,6,8,8-octamethyl-) (D4)*.

https://www.epa.gov/system/files/documents/2021-09/casrn_556-67-2-octamethylcyclotetra-siloxane-d4_draftscope_0.pdf

² ACC and SEHSC. (2020, January 28). *Request for Risk Evaluation under the Toxic Substances Control Act; Octamethylcyclotetrasiloxane (D4; CASRN: 556-67-2)*.

<https://www.regulations.gov/document/EPA-HQ-OPPT-2018-0443-0004>

permitted to expedite or otherwise provide special treatment to manufacturer-requested risk evaluations.³

D4 is a high production chemical, with an annual production volume of 750 million to 1 billion pounds according to the most recent 2016 CDR data. It has widespread application across industrial, commercial, and consumer uses including as a reactant to make other silicone chemicals; in adhesives, paints, and plastic products; and in food packaging and personal care products. Notably, over two decades, EPA has received 39 separate “substantial risk reports” on D4 from companies, highlighting health concerns such as reproductive toxicity and immunotoxicity.⁴

We support EPA’s progress here toward developing a more comprehensive chemical risk evaluation scope than previous risk evaluation scopes, in accordance with requirements and procedures under amended TSCA and the risk evaluation rule.⁵ Specifically, we commend EPA for indicating its intent to do the following:

- Assess exposures occurring via environmental releases to include fence-line exposures;
- Improve consideration of potential risks to workers by evaluating and making determinations of potential risk in the absence of personal protective equipment (PPE) as well as by including oral exposure via ingestion of particles;
- Include degradation byproducts of D4;
- Consider D4-contaminated food items in the evaluation of potential risk to the general population; and
- Evaluate combined exposures experienced by the general population and experienced by consumers.

However, as detailed in our comments below, EDF has concerns about the Draft D4 Scope, including the following:

- Failure to comprehensively identify specific “potentially exposed and susceptible subpopulations;”

³ TSCA Section 6(b)(4)(E)(ii)

⁴ These reports are required under TSCA Section 8(e): “Any person who manufactures, processes, or distributes in commerce a chemical substance or mixture and who obtains information which reasonably supports the conclusion that such substance or mixture presents a substantial risk of injury to health or the environment shall immediately inform the Administrator of such information unless such person has actual knowledge that the Administrator has been adequately informed of such information.”

⁵ 40 C.F.R. Part 702, Subpart B

- Absence of a revised systematic review method and peer reviewed systematic review protocol for D4;
- Inadequate commitment and plan to use information authorities under TSCA to fill the extensive data gaps identified;
- Failure to consider combined exposures to D4 experienced by workers occupationally (e.g., workers using multiple D4 products in the workplace) and experienced by individuals belonging to more than one receptor category (e.g., a worker who is also a member of a fenceline community);
- Lack of a commitment to include background exposures to D4 from non-TSCA uses (e.g., food packaging, personal care products, medical devices, and drugs);
- Insufficient detail on how uncertainty associated with the use of modeled or surrogate data will be assessed and integrated into evaluation of potential risks; and
- Inconsistent consideration of oral exposure to workers via hand-to-mouth behavior.

We urge EPA to address the identified concerns in the final D4 scope. Please see our detailed comments below.

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1. EPA has failed to provide a publicly available, peer-reviewed systematic review protocol.

Systematic review is defined as “a scientific investigation that focuses on a specific question and uses explicit, prespecified scientific methods to identify, select, assess, and summarize the findings of similar but separate studies.”⁶ Best practices in systematic review methodology dictate the creation, publication, and application of a pre-defined protocol *prior to the start of the systemic review* to minimize bias and increase transparency.⁷

Unfortunately, EPA has not approached the D4 scoping process in such a way. Contrary to best practices in systematic review, EPA has not provided a protocol for public comment as part of the Draft D4 Scope. Instead, EPA repeatedly refers to a “draft systematic review protocol” that will be made available for public comment and peer review “later this year”:

EPA plans to evaluate the epidemiological and toxicological literature for D4 using revised evaluation strategies that are described in a *draft systematic review protocol that EPA plans to release later this year for public comment and peer review*. (Draft D4 Scope, p. 11) (emphasis added)

The subsequent sections summarize the data collection activities completed to date for the general categories of sources and topic areas (or disciplines) using literature acquisition and screening methods as outlined in Appendix A and described in a *draft systematic review protocol that EPA plans to release later this year*. (Draft D4 Scope, p. 14) (emphasis added)

In 2018, EPA published the *Application of Systematic Review in TSCA Risk Evaluations* guidance document (TSCA SR method) to describe the agency’s approach to systematic review

⁶ IOM (Institute of Medicine). (2011). *Finding What Works in Health Care: Standards for Systematic Reviews*. Washington (DC): National Academies Press (US). DOI: [10.17226/13059](https://doi.org/10.17226/13059)

⁷ Woodruff, T.J., & Sutton, P. (2014). The Navigation Guide systematic review methodology: a rigorous and transparent method for translating environmental health science into better health outcomes. *Environ Health Perspect.*, 122(10). DOI: [10.1289/ehp.1307175](https://doi.org/10.1289/ehp.1307175)

in conducting risk evaluations under TSCA.^{8,9} The National Academies peer review report of the TSCA SR method called for broad changes to EPA’s approach to problem formulation and protocol development.¹⁰ Specifically, the committee called for better documentation of the process by which EPA engages in problem formulation and criticized the agency for not including a pre-specified protocol in their scoping documents.¹¹

While Appendices A-H provide the public details regarding the agency’s literature search methods and results to date, this is not the same as a comprehensive *a priori* “systematic review protocol.” Furthermore, EPA’s use of an unpublished “systematic review protocol” forces the public to comment on the Draft D4 Scope without full information. By proceeding in this manner, EPA jeopardizes the purpose of providing a draft scope for public comment.

More broadly, it is unclear what EPA means by the phrase “draft systematic review protocol” – a revised TSCA systematic review method¹² or a D4-specific systematic review protocol.

In accordance with principles of systematic review and recommendations from the National Academies, EPA should develop a D4-specific protocol and the public should be afforded an opportunity to comment on it as part of the scoping process. Separately, EPA must expeditiously release the revised TSCA SR method and provide opportunity for public comment. EPA is presumably applying a revised TSCA SR method to the 24 risk evaluations underway, and the public has no way of understanding how the revised method is shaping these risk evaluations.

At the very minimum, to the extent that EPA continues to move forward as indicated in the Draft D4 Scope, EPA must provide the public with the opportunity to comment on whatever is meant by “draft systematic review protocol” – expected to come out later this year – *prior to* EPA

⁸ U.S. EPA. (2018, May). Application of Systematic Review in TSCA Risk Evaluations. Retrieved October 25, 2021, from https://www.epa.gov/sites/default/files/2018-06/documents/final_application_of_sr_in_tsca_05-31-18.pdf

⁹ EDF. (2018, August 16). *Comments on Application of Systematic Review in TSCA Risk Evaluations*. <https://www.regulations.gov/document/EPA-HQ-OPPT-2018-0210-0077>

¹⁰ National Academies of Sciences, Engineering, and Medicine (NAS). (2021). The Use of Systematic Review in EPA’s Toxic Substances Control Act Risk Evaluations. *Washington, DC: The National Academies Press*. DOI: <https://doi.org/10.17226/25952>

¹¹ *Id.*

¹² In 2021, EPA committed to update and no longer use the TSCA SR method following a critical peer review by NAS. *See*: U.S. EPA. (2021, February). *Application of Systematic Review in TSCA Risk Evaluations*. <https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/application-systematic-review-tsca-risk-evaluations>

finalizing the D4 Scope.¹³ As part of the public comment opportunity, EPA should document any changes made to this draft protocol from the time it was initially applied.

2. Instead of relying on voluntary submissions of information, EPA must use their authority to fill data gaps.

EPA should make robust use of its TSCA information authorities to fill data gaps on D4. While EPA has made use of TSCA sections 4 and 8 for this chemical in the past, clear data gaps remain, as evidenced by the agency's requests to the public to voluntarily submit information throughout the Draft D4 Scope. To ensure that the agency has such information in sufficient time to incorporate into the draft risk evaluation, EPA should move swiftly to acquire this information through its TSCA authorities as soon as possible. Additionally, EPA should take advantage of other EPA programs, such as the Toxic Release Inventory Program within the Office of Pollution Prevention and Toxics, to fill information gaps.

A. EPA must not rely solely on voluntary information to fill data gaps.

Throughout the Draft D4 Scope, EPA requests information from the public. Specifically, EPA requests information from the public on (1) "environmental concentration of DMSD and the intermediate degradation products of D4 in water, soil, and sediment" (p. 36); (2) "dermal exposure of workers who handle articles containing D4 resulting from migration of D4 from these articles" (p. 37) (3) "worker and ONU inhalation exposure at landfills to D4 vapor and dust containing D4" (p. 37); and (4) any additional existing information, "such as full study reports or workplace monitoring from industry sources, that may be relevant to EPA's evaluation of conditions of use, exposures, hazards, and PESS during the risk evaluation." (p. 47)

While EDF supports broad information requests from the public, EPA should not rely exclusively on this approach to fill data gaps. EDF has previously commented on the significant limitations of relying on voluntary submission of information from industry, and we incorporate those comments here by reference.¹⁴ For example, a voluntary call is much less likely to produce all of the necessary information than are rules or orders mandating that affected parties provide the requested information. If manufacturers and processors are legally required to provide the information, that legal obligation provides a strong incentive for them to develop or obtain and submit all relevant information. Further, EPA has provided no empirical evidence establishing that a voluntary approach will result in EPA obtaining all "reasonably available" information.

¹³ See 40 C.F.R. § 702.41(c)(7)(i).

¹⁴ EDF. (2020, June 8). *Comments on Draft Scopes of the Risk Evaluations to Be Conducted for Seven Chemical Substances Under the Toxic Substances Control Act*, p. 50-53.
<https://www.regulations.gov/document/EPA-HQ-OPPT-2019-0131-0047>

This approach also runs the risk that EPA will not receive identified information from the public in a timely manner. EPA's information requests are not timebound, calling into question not only whether EPA would receive identified information in sufficient time to incorporate it into the risk evaluation, but also with enough time to obtain the requested information using its information authorities should the agency not receive the information voluntarily from the public. EPA will likely need to use its information authorities as the general public – not including the regulated community – is unlikely to have complete information across the data gaps identified. Effectively, EPA risks not obtaining all “reasonably available” information. To avoid such a situation, EPA must pair voluntary requests for information from the public with the use of its information authorities to fill identified data gaps.

B. EPA must use their information authorities to fill data gaps.

A constant criticism of EPA's risk evaluations for the first 10 chemicals was the dearth of information on which EPA relied to draw firm risk conclusions. Stakeholders like EDF¹⁵ and EPA's own Scientific Advisory Committee on Chemicals (SACC)¹⁶ have repeatedly pointed to the lack of sufficient, reliable information on the chemicals, including: their presence in and releases into various environmental media; their presence in and releases from industrial, commercial, and consumer products and materials; the extent and magnitude of workplace exposure levels; key human hazard endpoints; populations that are particularly highly exposed or susceptible; and ecological hazards to sediment- and soil-dwelling, terrestrial and aquatic organisms.

¹⁵ See e.g., EDF. (2019, October 11). *Comments on the Draft Risk Evaluation of 1-Bromopropane*. <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0235-0047>; EDF. (2020, April 27); *Comments on Draft Risk Evaluation of Trichloroethylene*. <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0500-0108>; EDF. (2019, August 30); *Comments on the 1,4-Dioxane Draft Risk Evaluation*. <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0238-0058>; and EDF (2019, December 30); *Comments on Draft Risk Evaluation of Methylene Chloride*. <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0437-0073>.

¹⁶ See, e.g., SACC. (2019, December 3-4). *Peer Review for EPA Draft Risk Evaluation for Methylene Chloride [Meeting Minutes and Final Report No. 2020-1]*. <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0437-0080>; SACC. (2019, September 10-12). *Peer Review for Draft Risk Evaluation for 1-Bromopropane (1-BP) [Meeting Minutes and Final Report No. 2019-03]*. <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0235-0061>; and SACC. (2019, July-August). *Peer Review for EPA Draft Risk Evaluations for 1,4-Dioxane and Cyclic Aliphatic Bromide Cluster (HBCD) [Meeting Minutes and Final Report No. 2019-02]*. <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0238-0063>

As EDF previously commented on the draft scopes for the next 20 risk evaluations, to avoid repeating this situation, EPA should make robust use of its information authorities to fill any gaps. We incorporate those comments by reference and briefly summarize them below.¹⁷

EPA should first clearly identify all significant information gaps on hazards or exposures, including those relevant to characterizing potential risks to potentially exposed or susceptible subpopulations.¹⁸ EPA must then use its authority under TSCA Section 4(a)(2) to require the development of new information to fill those gaps wherever possible. EPA must consider all information “reasonably available” to it,¹⁹ and information that EPA can generate under TSCA § 4(a)(2) qualifies as such under EPA’s own regulations as “information that EPA ... can reasonably generate [and] obtain ... for use.”²⁰ Thus, EPA should immediately identify such information gaps and then promptly require testing, including release or exposure monitoring, in a manner that allows it still to meet the statutory deadlines for risk evaluation.

TSCA Section 4(a)(2) provides EPA with authority to “require the development of new information relating to a chemical substance ... if the Administrator determines that the information is necessary ... to perform a risk evaluation under section 6(b).” In light of deadlines, EPA can and should use its order authority and does not need to make the additional findings required for a rule under TSCA Section 4(a)(1).

EPA should also promulgate reasonable regulations under Sections 8(d) and 8(a) to obtain information about hazards, exposures, and conditions of use, as well as exercise its authority under § 8(c) to obtain additional information. Consistent with TSCA section 8(a)(5), EPA can take steps to reduce unnecessary and duplicative reporting. Because TSCA requires EPA to conduct risk evaluations based on “reasonably available” information, and information available by exercising these authorities is “reasonably available” on its face, EPA must use these authorities to fulfill its duty. Collecting this information is also necessary to fulfill EPA’s duty to use the best available science, as required under TSCA Section 26(h).

TSCA Section 8(d) allows EPA to “require any person who manufactures, processes, or distributes in commerce ... any chemical substance or mixture ... to submit to the Administrator—lists of health and safety studies: (A) conducted or initiated by or for such person with respect to such substance or mixture at any time, (B) known to such person; or (C)

¹⁷ EDF. (2020, June 8). *Comments on Draft Scopes of the Risk Evaluations to Be Conducted for Seven Chemical Substances Under the Toxic Substances Control Act*, p. 50-53. <https://www.regulations.gov/document/EPA-HQ-OPPT-2019-0131-0047>

¹⁸ See 40 C.F.R. § 702.41(c).

¹⁹ TSCA Section 26(k)

²⁰ 40 C.F.R. § 702.33

reasonably ascertainable by such person.” EPA should issue Section 8(d) rules for D4. To obtain as complete a picture as possible, EPA should expressly require both manufacturers and processors to report on the chemical under the Section 8(d) rules.²¹

Further, EPA can use TSCA Section 11 information authority as necessary. Section 11 authorizes EPA to subpoena the production of reports, documents and other chemical information deemed necessary by the Administrator.

In the case of D4, EPA used its TSCA section 4 authority through an Enforceable Consent Agreement, as well as its section 8(d) authority, to obtain certain health and safety data.²² However, it is clear that data gaps remain. In addition to specific information requests EPA made of the public (see subsection 2-A above), literature inventory heatmaps in the draft scope identify several data gaps (see Draft D4 Scope, Figures 2-6, 2-8, and 2-10). For example, there is only one study on particle size characterization for occupational exposures (Draft D4 Scope, p. 20), one study on drinking water contamination (p. 22), and five human health studies (p. 24).

Furthermore, EPA’s new Public Information Curation and Synthesis (PICS) tool identifies a number of D4 information gaps on human and ecological hazards.²³ For example, the tool identified the following gaps in the publicly available information for D4: mammalian *in vivo* hazard data, subchronic and chronic information, as well as ecological *in vivo* acute plant and repeat dose invertebrate data.

In sum, EPA should aggressively use its TSCA information authorities to fill any data gaps considering information available in the literature and previously submitted to the agency. The Draft D4 Scope states, “For any data needs *identified during the risk evaluation*, EPA may use the Agency’s TSCA authorities under sections 4, 8, or 11, as appropriate.” (p. 47, emphasis added) Instead, EPA should use these information authorities *now* to ensure that submitted information can be incorporated into the draft risk evaluation made available for public comment and for peer review by the SACC.

²¹ See 40 C.F.R. § 716.5(c).

²² EPA received five ecotoxicity studies, three environmental fate studies, and two water solubility studies through the test rule. EPA also received one reproductive toxicity test and one environmental monitoring study under 8(d), as well as 39 Substantial Risk Reports under 8(e) (Draft D4 Scope, Appendix D.1).

²³ U.S. EPA. (2021, June). *A Proof-of-Concept Case Study Integrating Publicly Available Information to Screen Candidates for Chemical Pre-Prioritization under TSCA*. <https://awsedap.epa.gov/public/single/?appid=bbe9d633-5fe5-4455-8212-8a4e5aa0cd34&sheet=c76264da-6678-4ebd-ae78-acc8b13a15a7>

C. EPA should add D4 to the Toxic Release Inventory (TRI).

EPA indicates in the Draft D4 Scope that the agency intends to rely on modeled values and surrogate data to impute missing data throughout the D4 risk evaluation. As discussed above, EPA should expediently exercise its information authorities to eliminate existing data gaps, in part to reduce the uncertainty that results from EPA reliance on modeled or surrogate data. In addition to using its information authorities under TSCA, EPA can also leverage its authorities under other statutes to help fill information gaps.

In the Draft D4 Scope, EPA makes clear that direct releases to the environment are crucial inputs to exposure models – demonstrating why D4, and any other chemical undergoing risk evaluation, ought to be added to Toxic Release Inventory (TRI). The addition of D4 to the TRI should be done in a timeframe that provides information that can be incorporated into the risk evaluation. If immediately initiating the addition of D4 to TRI will not yield information before EPA completes the D4 risk evaluation, TRI-provided environmental release data will still be very useful for other reasons, such as for monitoring and enforcement-related activities associated with risk management, as well as to assist other authorities (e.g., federal, state, region, and tribal governments) and members of the public who may need media-specific D4 waste management data for their own purposes.

3. EPA does not have discretion to pick and choose conditions of use.

A. Section 3(4) does not grant EPA authority to pick and choose among relevant conditions of use.

EPA has stated in the Draft D4 Scope that TSCA Section 3(4) “grants EPA discretion to determine the circumstances that are appropriately considered to be conditions of use for a particular chemical substance.” (p. 29) This position is contrary to the Ninth Circuit’s decision that EPA’s regulations (40 C.F.R. § 702 Subpart B) do not grant the agency discretion to exclude conditions of use from the scope of risk evaluations.²⁴ Petitioners in that case had challenged EPA’s Risk Evaluation Rule (“Rule”) as apparently granting EPA discretion to exclude conditions of use from risk evaluations. The Court ruled that “the challenged provisions unambiguously do *not* grant EPA the discretion Petitioners contend.”²⁵

The court determined that the Rule’s phrase “the conditions of use within the scope of” an evaluation simply refers to the conditions of use that are applicable to any particular substance—and that therefore are included in the scope of that substance’s evaluation—without excluding

²⁴ *Safer Chemicals v. United States EPA*, 943 F.3d 397 (9th Cir. 2019)

²⁵ *Id.* at 419 (emphasis added)

any conditions of use in forming that list [of conditions of use].”²⁶ Further, while the preamble to the Rule stated that EPA did retain discretion to exclude conditions of use, the Court found that “because the scope provisions are not ambiguous on their face, reference to the preamble discussion would be improper.”²⁷

EPA must comply with the Court’s well-considered interpretation of the Rule.²⁸ And the Court found no ambiguity in the Rule, which forecloses EPA from interpreting the Rule in a different way. As a result, EPA must consider all conditions of use when preparing risk evaluations, including for D4.

B. EPA wrongfully excluded spills and leaks as a condition of use.

In the Draft D4 Scope, EPA indicates that spills and leaks are outside of the scope of the D4 risk evaluation: “EPA assumes transportation of D4 is in compliance with existing regulations for the transportation of hazardous materials, and emissions are therefore minimal (*with the exception of spills and leaks, which are outside the scope of the risk evaluation*).” (p. 32, emphasis added) However, exposures from leaks and spills in the workplace could be a substantial source of exposure, especially considering the potential for inhalation exposure from evaporation.

EDF previously commented that leaks and spills constitute a “reasonably foreseen ... circumstance under which a chemical is manufactured, processed, distributed, used or disposed of” and lead to exposures that need to be considered in a risk evaluation.” Congress included “reasonably foreseen” circumstances within TSCA’s reach with the express goal of ensuring that EPA swept more broadly than considering only known (or intended) uses. Further, in the tort context, courts have determined that spills and leaks can be reasonably foreseen.²⁹ We incorporate our previous comments by reference.³⁰

4. EPA must consider all exposure pathways, even where those pathways may be regulated under other EPA authorities.

In the past, EPA asserted that it has discretion to exclude “various media pathways (i.e., air, water, land) [that] fall under the jurisdiction of existing regulatory programs and associated

²⁶ *Id.*

²⁷ *Id.* at 420.

²⁸ See TSCA Section 6(b)(4)(C) (requiring EPA to conduct risk evaluations “in accordance with [the Rule]”).

²⁹ See, e.g., *Lumbermens Mut. Cas. Co. v. Banco Espanol De Credito*, 2006 U.S. Dist. LEXIS 75728, at *25 (S.D.N.Y. Oct. 13, 2006) (describing leak as reasonably foreseeable).

³⁰ EDF. (2020, April 27). *Comments on Draft Risk Evaluation of Trichloroethylene*, p.36-37. <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0500-0108>

analytical processes carried out under other EPA-administered statutes and have been assessed and effectively managed under those programs.”³¹ In June 2021, EPA acknowledged that the “first 10 risk evaluations [including 1,4-dioxane] did not assess air, water or disposal exposures to the general population because these exposure pathways were already regulated, or could be regulated, under other EPA-administered statutes such as the Clean Air Act, Safe Drinking Water Act, or Clean Water Act” and announced important policy changes to address the flaws with such an approach.³²

EDF is very heartened by EPA’s announcement that the agency would include all environmental pathways of exposure in its risk evaluations under TSCA, commensurate with requirements under the law. However, in the Draft D4 Scope, it seems the agency has applied the same flawed logic it criticized earlier this year. Specifically, in Figure 2-11, “EPA assumes transportation of D4 is in compliance with existing regulations for the transportation of hazardous materials, and emissions are therefore minimal (with the exception of spills and leaks, which are outside the scope of the risk evaluation).” (p. 32)

Additionally, although EPA does include most environmental exposure pathways (i.e., land, water, and air) in their exposure analysis plan, it is unclear if EPA has abandoned their previous practice of excluding pathways governed by other statutes, as EPA indicated that they would do in their summer announcement, or simply included such pathways because D4 is not governed by other environmental statutes. We strongly recommend that EPA explicitly state the agency’s policy to include all relevant exposures pathways – regardless of regulatory jurisdiction – in the final scope, both generally for TSCA risk evaluations and specifically for D4.

Furthermore, Appendix A-7 (“Pathways Identified as Supplemental for D4”) indicates that EPA intends to treat environmental pathways addressed by other EPA-administered statutes as “supplemental pathways” which, EPA states, “refer to pathways addressed by other EPA administered statutes. Studies tagged under these pathways provide media information that is not prioritized in the screening process. (Draft D4 Scope, p. 81)

EDF urges EPA to abandon the notion that environmental pathways addressed by other EPA-administered statutes should be considered as secondary to, or lower priority than, other pathways. EPA must include and give equal treatment to all environmental pathways of D4 exposure in the final scope and risk evaluation. The notion that EPA can exclude or deprioritize

³¹ U.S. EPA. (2018, May). *Problem Formulation for 1,4-Dioxane*. https://www.epa.gov/sites/default/files/2018-06/documents/14-dioxane_problem_formulation_5-31-18.pdf

³² U.S. EPA. (2021, June 30). *EPA Announces Path Forward for TSCA Chemical Risk Evaluations*. <https://www.epa.gov/newsreleases/epa-announces-path-forward-tsca-chemical-risk-evaluations>

an environmental exposure pathway or condition of use based on the existence of other statutes is inconsistent with the law and results in, according to EPA itself, “a failure to consistently and comprehensively address potential exposures to potentially exposed or susceptible subpopulations, including fenceline communities (i.e., communities near industrial facilities).”³³ Nothing in TSCA’s risk evaluation provision, nor in EPA’s risk evaluation rule, authorizes EPA to ignore exposures because of other statutory authorities.

Several other provisions of TSCA also indicate that Congress intended for EPA to consider such exposures, and these provisions – including Sections 3(4) and 6(b)(4)(A) – are discussed in detail in EDF’s earlier comments on the major flaws underlying EPA’s statutory exclusions.^{34, 35} EDF incorporates those comments by reference and reiterates those arguments. Here, EDF will briefly summarize two of the problems with the statutory exclusions.

First, regulation under laws other than TSCA may reduce, but do not eliminate, releases of chemicals to the environment. If EPA were to exclude known exposures to D4 from its releases into various environmental media, EPA would effectively be assuming that those releases and the associated risks are zero (i.e., non-existent), despite the fact that available evidence EPA cited establishes that environmental releases at levels well above zero are occurring.³⁶ These releases are occurring even accounting for any actions EPA has taken under the other statutes it invokes.

Second, such an interpretation fails to acknowledge that requirements under other laws to address human and environmental health risks derive from statutes that establish criteria different than those under TSCA.³⁷ Many of these other statutes, for example, require EPA or other agencies to consider factors such as cost and feasibility when setting standards – factors that TSCA explicitly forbids EPA from taking into account when assessing risks. TSCA Section 6(b)(4)(A) states (emphasis added):

³³ *Id.*

³⁴ EDF. (2019, August 16). *Comments on Ten Problem Formulations under the Toxic Substances Control Act*, p. 23-55. <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0741-0085>

³⁵ EDF. (2020, April 27). *Comments on Draft Risk Evaluation of Trichloroethylene*, p. 36-37. <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0500-0108>

³⁶ We note that the Negotiated Enforceable Consent Agreement for monitoring certain cyclic siloxane chemicals includes information on D4’s presence in industrial effluent. Available at: <https://www.regulations.gov/docket/EPA-HQ-OPPT-2012-0209>

³⁷ EDF has addressed these limitations in greater detail in prior comments. *See, e.g.*, EDF. (2020, April 27). *Comments on Draft Risk Evaluation of Trichloroethylene*. <https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0500-0108>

The Administrator shall conduct risk evaluations pursuant to this paragraph to determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, *without consideration of costs or other nonrisk factors*, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator, under the conditions of use.

5. EPA must fully account for exposure through food consumption in all exposure settings.

Although EPA considered contaminated food as a source of D4 exposure in Section 2.3.7 on “General Population Exposures,” food is not mentioned in the “Occupational Exposures” (Section 2.3.5) or “Consumer Exposures” (Section 2.3.6) sections. It is unclear why EPA does not consider and classify exposure through food to be an occupational or consumer exposure, as food is clearly consumed by people in both workplace and consumer exposure settings; and thus, constitutes a relevant exposure route for these groups. The final D4 scope should include consumption of food by consumers and workers – a potentially exposed or susceptible subpopulation – in addition to the general population.

In occupational exposure settings, some workers may well eat or drink while actively working. But even when this is not the case, most workers in and around where chemicals are manufactured, processed, or used will take breaks to use the restroom, eat lunch, and engage in other such activities. Workers may not carefully wash their face and hands or change out of their contaminated clothes for each break or at the end of the day. And they may touch surfaces on which a chemical, especially if it is not volatile, may settle. During each of these activities, workers may transfer a chemical to food they then consume or may engage in some other hand-to-mouth activities that result in ingestion.

Like workers, consumers of products containing D4 may also be exposed orally “through product use via transfer from hand to mouth.” (Draft D4 Scope, p. 37) Thus, exposure through food is also a concern for consumers who may unintentionally transfer D4 residues from their hands to their mouth by handling food after handling a D4-containing product.

6. EPA must consider background exposure levels from non-TSCA conditions of use.

D4 has a variety of non-TSCA uses, including food packaging materials, personal care products or cosmetics, and medical devices and drugs. While we are encouraged that EPA has stated in the Draft D4 Scope that it *may* consider the potential D4 exposures from “non-TSCA uses” and that “the potential exposures of non-TSCA uses may help inform the Agency’s risk determination for the exposures from uses that are covered under TSCA” (p. 30), EPA has unfortunately categorized these non-TSCA uses as “activities excluded from the scope of the risk evaluation.” (Draft D4 Scope, p. 29) This flies in the face of people’s lived reality, as any potential health

effects from exposure to D4 are a function of a person’s total exposure to the chemical, regardless of source, and regardless – of course – what federal law is implicated. This is also inconsistent with manufacturers’ request to EPA for a risk evaluation of D4, which put forth the following:³⁸

Uses in food contact materials, cosmetics and personal care products, and over the counter medication (OTC) do not fall under TSCA but are governed by other regulations and are technically not included in a TSCA risk evaluation. However, these uses are considered in Section 5.1 of the Exposure Assessment as a conservative approach. (p. 47)

EPA should explicitly commit to considering background exposures from non-TSCA uses in the final D4 scope. Failure to consider exposures from those uses would be arbitrary and capricious, and inconsistent with scientific standards and weight of the scientific evidence requirements established in TSCA Sections 26(h) and (i). While EPA may not be able to directly regulate non-TSCA uses, EPA cannot adequately evaluate the conditions of use that are subject to TSCA regulation, or control their unreasonable risks, if the agency ignores relevant background sources of exposure. If EPA ignores such D4 exposures, the D4 risk evaluation will underestimate exposure and risk, and inhibit the agency’s ability to protect public health.

If a chemical is found to present an unreasonable risk through the risk evaluation process after accounting for all exposure sources, then risk management can and should take into account how much of that risk derives from different sources and which sources are best managed under TSCA or under a different authority. Section 9 of TSCA directly provides for this potential delegation of authority – but only *after* completion of a TSCA risk evaluation that comprehensively considers exposure to a chemical.

Below, we discuss the importance of each background source of exposure:

Food contact materials and additives: D4 is “listed as an optional substance to be used in food packaging material” and “approved for food use as an antifoaming agent in pre- and post-harvest.” (Draft D4 Scope, p. 30, 101) A 2017 industry-funded risk assessment (Gentry et al., 2017) concluded that relevant exposure pathways for D4 also include “use of baby bottle nipples, pacifiers, and sipper tubes manufactured from silicone polymers” and “ingestion of residual antifoam present in processed food.”

Personal care products: D4 has been detected in personal care products such as antiperspirants, skin care products (e.g., sunscreen, lotion, aftershave, and make-up), and hair care products (e.g.,

³⁸ ACC and SEHSC. (2020, January 28). *Request for Risk Evaluation under the Toxic Substances Control Act; Octamethylcyclotetrasiloxane (D4; CASRN: 556-67-2)*, p. 47. <https://www.regulations.gov/document/EPA-HQ-OPPT-2018-0443-0004>

shampoo, conditioner, and hair spray).³⁹ In 2016, the European Chemicals Agency (ECHA) Committee for Risk Assessment concluded that D4 should be restricted in “personal care products that are intended to be used or disposed with water, e.g., shower gels, shaving foams and shampoos” due to its effect on the aquatic environment in the EU.⁴⁰ In addition, Gentry et al. (2017) “determined from the Monte Carlo analysis that in all cases, specific personal care product use (body lotion, hair spray, foundation, after shave and APs) by adults provided the highest contribution to potential D4 exposure,” compared to other, environmental media (e.g., ingestion of water, soil, air, fish, and other foods) (Gentry et al., 2017, p. 34). The risk assessment also highlighted the vulnerability of certain occupational groups such as barbers and beauticians as a result of regular application of D4-containing hair care products.

Medical devices and drugs: D4 is used in medical devices such as dental bonding agents and breast implants (Draft D4 Scope, p. 30), as well as over-the-counter medications such as vapor rub and anti-gas medications.⁴¹ According to Health Canada’s screening assessment of D4, “[s]ilicone elastomers are also used in a large number of biomedical applications including short- and long-term implants and prostheses, catheters, contact lenses and dentures (Will et al., 2007).”⁴² ECHA found that silicones such as D4 can migrate from silicone-based breast implants into the body, especially in the case of a rupture or leak.⁴³ Additionally, oral ingestion of D4 via some over-the-counter medications is expected.⁴⁴

³⁹ Gentry, R., Franzen, A., Landingham, C.V., Greene, T., & Plotzke, K. (2017). A global human health risk assessment for octamethylcyclotetrasiloxane (D4). *Toxicology Letters*. <https://doi.org/10.1016/j.toxlet.2017.05.019>

⁴⁰ European Chemical Agency (ECHA), Committee for Risk Assessment (RAC). (2016, March 10). *Opinion on an Annex XV dossier proposing restrictions on OCTAMETHYLCYCLOTETRASILOXANE, DECAMETHYLCYCLOPENTASILOXANE*. <https://echa.europa.eu/documents/10162/83df6e5b-e7ae-8279-ed47-e6d92912721c>

⁴¹ ACC and SEHSC. (2020, January 28). *Request for Risk Evaluation under the Toxic Substances Control Act; Octamethylcyclotetrasiloxane (D4; CASRN: 556-67-2)*, p. 61. <https://www.regulations.gov/document/EPA-HQ-OPPT-2018-0443-0004>.

⁴² Health Canada. (2008, November). *Screening Assessment for the Challenge Octamethylcyclotetrasiloxane (D4)*, p. 9. https://www.ec.gc.ca/ese-ees/2481B508-1760-4878-9B8A-270EEE8B7DA4/batch2_556-67-2_en.pdf

⁴³ European Commission, Scientific Committee on Emerging and Newly Identified Health Risks. (2014, May). *The safety of Poly Implant Prothèse (PIP) Silicone Breast Implants – Update of the Opinion of February 2012*. https://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_043.pdf

⁴⁴ Health Canada. (2008, November). *Screening Assessment for the Challenge Octamethylcyclotetrasiloxane (D4)*, p. 27. https://www.ec.gc.ca/ese-ees/2481B508-1760-4878-9B8A-270EEE8B7DA4/batch2_556-67-2_en.pdf

In sum, we urge EPA to consider D4 exposures from food contact materials and additives, personal care products and cosmetics, and medical devices and drugs as background exposures. Specifically, in the final D4 scope, EPA should unequivocally (1) state its plans to include such background exposures in the final version of the scope, (2) update the study search and screening criteria to capture information related to background D4 exposure, and (3) examine risks to individuals across the population who are particularly vulnerable to background exposures by nature of their occupation or behavior, including but not limited to infants, barbers, beauticians, and women with silicone-based breast implants.

Further, we recommend that EPA coordinate with other executive agencies (e.g., FDA, Consumer Product Safety Commission, Agency for Toxic Substances and Disease Registry, National Institute of Environmental Health Sciences) to obtain information about D4 that could inform EPA's assessment of background exposures. To reiterate, TSCA Section 9 describes procedures for coordinating with other federal agencies with respect to risk evaluation and risk management considerations relating to non-TSCA conditions of use.

7. EPA must account for, and acquire, information needed to accurately evaluate real-world occupational exposures.

The Draft D4 Scope demonstrates EPA's intention to make several improvements in estimating risk to workers, including a commitment to analyze worker exposure without personal protective equipment (PPE) and make risk determinations in the absence of PPE. This is a marked improvement from the Trump Administration's risk evaluations. The Draft D4 Scope also hints at including the oral route of exposure for workers, which was previously ignored across the first 10 risk evaluations.

While EDF commends EPA for making these improvements, the agency must go further in the final D4 scope and in the D4 risk evaluation to reflect real-world occupational exposures. Specifically, EPA should include hand-to-mouth behavior in the workplace leading to direct ingestion, more accurate inhalation exposure modeling for occupational non-users, and – where EPA analyzes PPE – it should include consideration of PPE's limited efficacy.

A. Oral exposure route

EPA's consideration of the oral exposure route for workers is a welcome development, as this route of exposure was entirely ignored for workers under the first 10 risk evaluations. EPA recognizes that oral exposure may occur both via inhaled particles that deposit in the respiratory tract and direct ingestion from hand to mouth behavior. However, the Draft D4 Scope indicates that the agency will consider direct ingestion only on a "case-by-case basis" and "may assess oral exposure for workers for certain [conditions of use] and worker activities where warranted." (p. 37) Furthermore, this exposure route is not reflected in the Conceptual Model (Draft D4 Scope, Figure 2-13), as oral exposure is not included in EPA's "Liquid/Solid Contact" pathway,

and in several other locations in the D4 Draft Scope, EPA omits the oral route of exposure when describing the analysis plan for workers and occupational non-users (e.g., p. 10).

Direct ingestion should be systematically considered. Ng et al. (2014) assessed inadvertent hand- and object-to-mouth behavior among workers for use in exposure modeling and found that, on average, workers had contact frequencies of 6.3 per hour; these frequencies were much higher when workers were between tasks (23.5 contacts per hour).⁴⁵ The authors also found that use of PPE such as gloves did not impact the contact frequency, and that this route of exposure was particularly important for workers who smoke or bite their nails. As discussed previously (Section 5), workers may also directly consume contaminated food in the workplace due to eating on the job or touching food with contaminated hands during breaks.

B. Personal protective equipment (PPE) assumptions

Consistent with EPA's June 30, 2021 announcement,⁴⁶ the Draft D4 Scope indicates EPA's plan to make risk determinations based on analyses that do not assume use of PPE by workers. We applaud this approach, given that workplaces are not universally compliant with OSHA standards and given the considerable evidence of major real-world limitations of PPE regarding its effectiveness and the true extent of its use by workers. EDF has commented extensively on this issue in the past.⁴⁷

The Draft D4 Scope specifically states: "EPA will not make risk determinations based on assumptions about the use of personal protective equipment (PPE) or control technologies. However, EPA plans to develop exposure scenarios with and without the use of PPE and engineering controls to inform any potential risk management required subsequent to an unreasonable risk determination for workers or ONUs." (Draft D4 Scope, p. 36)

When assessing exposure with the use of PPE for future risk management, EPA should take into account PPE's limited efficacy even when its use is required. PPE shifts the burden of protection from harm onto the workers themselves, who may not be able to wear the equipment properly

⁴⁵ Ng, M. G., Davis, A., van Tongeren, M., Cowie, H., & Semple, S. (2014). Inadvertent ingestion exposure: hand- and object-to-mouth behavior among workers. *J. of Exp Sci & Environ Epi*, p. 9-16. <https://www.nature.com/articles/jes201471>

⁴⁶ U.S. EPA. (2021, June 30). *EPA Announces Path Forward for TSCA Chemical Risk Evaluations*. <https://www.epa.gov/newsreleases/epa-announces-path-forward-tsca-chemical-risk-evaluations>

⁴⁷ EDF. (2020, June 8). *Comments on Draft Scopes of the Risk Evaluations to Be Conducted for Seven Chemical Substances Under the Toxic Substances Control Act*, p. 56-58. <https://www.regulations.gov/document/EPA-HQ-OPPT-2019-0131-0047>

due to a number of factors. For example, a 2016 OSHA letter to EPA explained these challenges with respect to respirators:

[T]o be effective, respirators must be individually selected, fitted and periodically refitted, conscientiously and properly worn, regularly maintained, and replaced as necessary. The absence of any one of these conditions can reduce or eliminate the protection the respirator provides.

Respirator effectiveness ultimately relies on the practices of individual workers who must wear them. ... Furthermore, respirators can impose substantial physiological burdens on workers, including the burden imposed by the weight of the respirator; increased breathing resistance during operation; limitations on auditory, visual, and olfactory sensations; and isolation from the workplace environment.⁴⁸

Furthermore, OSHA's database of inspections demonstrates significant noncompliance with OSHA respiratory protection requirements. For example, in fiscal years 2018 and 2019, OSHA cited nearly 3,000 violations each year of the respiratory protection standard, identified in nearly 1,300 separate inspections each year.⁴⁹ Violations of the respiratory standard were the 4th most common type of violation in OSHA inspections in fiscal year 2018, exceeded only by violations for two categories of physical hazard and the Hazard Communication Standard.⁵⁰

EPA should obtain the information needed to account for such real-world limitations of PPE by collecting or requiring the development of empirical data needed to assess the actual extent of the use of PPE and the resulting exposure reduction. Obtaining and utilizing such data is necessary to proceed in a "manner consistent with best available science" (a requirement under

⁴⁸ Michaels, D.M. (2016, October 28). *Comment submitted by David Michaels, PhD, Occupational Safety and Health Administration (OSHA)*.

<https://www.regulations.gov/document?D=EPA-HQ-OPPT-2014-0650-0041>

⁴⁹ In FY 2018, OSHA reported 2,892 violations identified in 1,281 inspections. In FY 2019, OSHA reported 2,932 violations identified in 1,289 inspections. While citations reduced in FY20 (1,528), there were only half the number of inspections (644). The FY 2020 statistics are available at U.S. Department of Labor, OSHA. (n.d.). *Industry Profile for OSHA Standard 19100134*. Retrieved October 19, 2021 from https://www.osha.gov/pls/imis/industryprofile.stand?p_esize=&p_stand=19100134&p_state=FE%20Federal&p_type=5. The FY 2018 and FY 2019 statistics were recorded by EDF earlier and have since been replaced with the FY 2020 data and appear to no longer be accessible.

⁵⁰ U.S. Department of Labor, OSHA. (n.d.). *Top 10 Most Frequently Cited Standards*. Retrieved on October 25, 2021 from <https://www.osha.gov/top10citedstandards>

TSCA Section 26), and EPA has clear authority to collect or require the development of such data under TSCA Section 4(b)(2)(A). EPA should start by examining the eight PPE occupational exposure studies identified through the literature search in Figure 2-6 of the Draft D4 Scope.

C. Inhalation exposure to occupational non-users

EPA's proposed approach for estimating inhalation exposure to occupational non-users will underestimate exposure to this population, as it assumes that they will always stay outside of the near-field zone of the chemical's use (see Section 11-C for further detail). EPA cannot make this assumption in the absence of empirical information indicating this is true. To the extent possible, EPA should acquire information on the location of occupational non-users for specific conditions of use and at a minimum use a more conservative default assumption.

8. EPA has failed to identify specific potentially exposed or susceptible subpopulations.

TSCA Section 6(b)(4)(D) requires that EPA consider "potentially exposed or susceptible subpopulations" when evaluating chemicals. EPA's implementing regulations also require EPA to identify these subpopulations in the draft scopes it provides for public comment.⁵¹ In comparison to previous scopes, the Draft D4 Scope lists "bystanders, and indigenous, native populations" as groups that will be considered by EPA as potentially exposed or susceptible subpopulations (p. 40). EPA also states in the Draft D4 Scope that it "plans to increase consideration of environmental justice" in their risk evaluations (p. 40). EDF supports EPA's inclusion of these groups as potentially exposed or susceptible subpopulations and stated commitment to environmental justice.

Although EPA has specified some potentially exposed or susceptible subpopulations in the Draft D4 Scope – an improvement – EPA's identification of subpopulations is not comprehensive. Indeed, the language in the draft scope remains very similar to language from previous scoping documents. EPA provides four paragraphs, consisting of largely boilerplate language, on potentially exposed or susceptible subpopulations, instead of identifying specific subpopulations. In section 2.5 of the Draft D4 Scope, EPA merely quotes TSCA's definition of the term and repeats EPA's earlier identification at the prioritization stage of the broad categories of "children, women of reproductive age (e.g., pregnant women), consumers and workers" as comprising such subpopulations (p. 40). Furthermore, rather than list specific groups of people, EPA states that it "plans to analyze reasonably available information in order to determine whether some human receptor groups may be exposed via exposure pathways that may be distinct to a particular subpopulation or life stage." (p. 40)

Specifically, EPA failed to identify specific populations that live, work, learn, play, and/or worship in proximity to conditions of use and sources of contamination, also known as

⁵¹ 40 C.F.R. § 702.41

“fenceline communities,” as potentially exposed or susceptible subpopulations. These communities are at a heightened risk of exposure to D4 and constitute a “potentially exposed and susceptible subpopulation” under TSCA. While EPA does discuss performing “fenceline analysis where appropriate to screen for potential effects with emphasis on PESS and environmental justice communities” (Draft D4 Scope, p. 40), EDF is concerned about the agency’s non-committal language surrounding fenceline analysis, as these analyses are not only *always* appropriate, but also legally required.

Among other sources of information, fenceline communities relevant to the D4 risk evaluation can be identified using EPA-collected data. While D4 is not a TRI chemical, which is problematic for the reasons discussed in Section 2-C, EPA can leverage data collected under the Chemical Data Reporting Rule (CDR) to identify D4 manufacturing and importing sites across the country. All communities surrounding such sites are by definition fenceline communities and thus constitute “potentially exposed and susceptible subpopulations” under TSCA. If EPA intends to effectively characterize potential fenceline risk and ultimately advance environmental justice, the agency must assess all relevant fenceline communities.

Additionally, in the Draft D4 Scope, EPA indicates that studies that identify potentially exposed or susceptible subpopulations during the literature screening process, but do not evaluate health outcomes, were tagged as supplemental material (p. 15). This is problematic. All studies bearing on potentially exposed or susceptible subpopulations should be considered primary evidence, not a lesser category of supporting information. Regardless of whether these studies provide information about health outcomes, they could provide valuable exposure-relevant information.

In sum, in the final D4 scope, EPA should identify specific potentially exposed or susceptible subpopulations it intends to include in the risk evaluation, including but not limited to fenceline communities, and include information on these groups as primary evidence rather than supplemental information.

9. EPA’s study inclusion criteria for D4 should include all relevant information.

EPA states that studies on “[m]easurement of exposure concentrations resulting from a chemical spill” and “[m]easurement of exposure due to food processing components, medications, or use of anti-perspirants” do not meet the screening criteria and, as a result, are excluded (Draft D4 Scope, p. 25). As described above, exposure to D4 resulting from chemical spills or leaks (Section 3-B), as well as from “background exposures” such as food packaging, personal care products, and medical applications (Section 6), should be considered within the scope of the risk evaluation. Therefore, inclusion criteria in the final D4 scope should reflect associated sources of information. In the final D4 scope, EPA should revise the screening criteria to include all relevant information that could be used during the risk evaluation consistent with TSCA’s requirement to use all information that is “reasonably available to the Administrator.”⁵²

⁵² TSCA Section 26(k)

Further, EPA states that “[t]he potential exposures of non-TSCA uses may help inform the Agency's risk determination for the exposures from uses that are covered under TSCA (e.g., as background exposures that would be accounted for....)” (Draft D4 Scope, p. 30). Thus, studies that measure exposures from background sources including food packaging materials, personal care products, and medical items are relevant and should be reflected in the inclusion criteria for data sources and information. We provide greater discussion on the inclusion of background exposures in Section 6.

10. EPA should provide greater detail regarding its approach to uncertainty in the final D4 scope.

We argue the best way to reduce uncertainty from reliance on modeled or surrogate data is to attain measured data, and we describe in Section 2 the authorities that EPA should use to gather measured data and other information. To the extent that EPA does choose to fill any remaining information gaps with modeled or surrogate data, the following points ought to be considered.

EPA provides insufficient detail regarding how it intends to conduct requisite uncertainty analyses. Lack of assessment of uncertainty in past draft risk evaluations has been criticized by the Scientific Advisory Committee on Chemicals (SACC) as insufficient.⁵³ Among other concerns, in their peer review of the 1,4-dioxane and HBCD draft risk evaluations, the SACC told EPA that “uncertainty in the estimates presented for environmental exposures needs to be addressed.”⁵⁴ To address concerns the SACC had with past draft risk evaluations, it is imperative that EPA outline the steps it plans to take to account for uncertainty in its modeled estimates in the final D4 scope so EPA is prepared to implement such steps in the draft risk evaluation.

A. EPA must conduct uncertainty analysis when using models.

EPA’s planned reliance on models in the D4 risk evaluation is extensive. The agency indicates that it plans to use models to estimate physical chemical and environmental fate and transport properties, as well as environmental, consumer, and general population exposures (Draft D4 Scope, Section 2.7). EPA states that it plans to use the Chemical Screening Tool for Exposures and Environmental Releases (ChemSTEER) “to augment and/or supplement [environmental release] data through the use of models and potential surrogate data where appropriate.” (p. 48) In addition, EPA states that it will use OPPT’s Indoor Environmental Concentrations in

⁵³ SACC. (2019, December 3-4). *Peer Review for EPA Draft Risk Evaluation for Methylene Chloride [Meeting Minutes and Final Report No. 2020-1]*.

<https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0437-0080>

⁵⁴ SACC. (2019, July-August). *Peer Review for EPA Draft Risk Evaluations for 1,4-Dioxane and Cyclic Aliphatic Bromide Cluster (HBCD) [Meeting Minutes and Final Report No. 2019-02]*.

<https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0238-0063>

Buildings with Conditioned and Unconditioned Zones (IECCU) model, Consumer Exposure Model (CEM), and other similar models to estimate indoor air exposures from various sources.

EPA cites EPI Suite for estimated physical chemical property values (Draft D4 Scope at Appendix C). However, physical-chemical property models in EPI Suite lack transparency in performance and applicability. While performance of the individual property estimation methods used in EPI Suite are available in the EPI Suite™ help files, the property model performance estimations are only presented in terms of overall performance and do not describe whether or not the model is applicable for any specific chemical.⁵⁵ For example, the accuracy and domain section in the help file for KOWWIN (the Log Octanol-Water Partition Coefficient Program) describes the domain for the model as having "no universally accepted definition..." and that the user "may wish to consider the possibility" that property estimates are less accurate for compounds with molecular weights higher or lower than those used in the training set. Similar disclaimer statements are found in each program that uses quantitative structure property relationships (QSPR). The newer QSPR model, EPA's OPEn structure-activity/property Relationship App (OPERA), includes the reporting of a chemical-specific applicability domain, and was built using a newer database of physical-chemical parameters.⁵⁶ It is unclear if EPA will use this newer, more transparent model for its estimation of physical-chemical properties.

Additionally, the Analysis Plan presented in the Draft D4 Scope indicates EPA's intention to assess inhalation exposure through a two-zone (near-field/far-field model), with the near-field exposure representing potential inhalation exposure to workers, and the far-field exposure representing potential inhalation exposure to Occupational Non-Users (ONUs) (p. 52). In EPA's first 10 risk evaluations, the agency likewise assumed that workers would spend the entire duration of the activity in their respective exposure zones. This assumption was criticized by the SACC. For example, during the 1-BP peer review meeting, one SACC member with industrial hygiene experience noted that workers and ONUs may regularly pass into each other's space, e.g., to communicate or otherwise interact.⁵⁷ This approach will likely underestimate exposure ONUs.

⁵⁵ "The classical approach of comparing models by global R^2/Q^2 fitting performance may or may not reflect higher predictive ability, especially when dealing with different sizes of datasets, for example. Therefore, comparisons of model fit should be local and specific, not based on overall statistics." Mansouri K, Grulke CM, Judson RS, Williams AJ. (2018). OPERA models for predicting physicochemical properties and environmental fate endpoints. *J Cheminform.* 10(1):10. doi:10.1186/s13321-018-0263-1

⁵⁶ *Id.*

⁵⁷ SACC. (2019, September 10-12). *Peer Review for Draft Risk Evaluation for 1-Bromopropane (1-BP) [Meeting Minutes and Final Report No. 2019-03]*, p. 27-28.
<https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0235-0061>

Despite the many models referenced in the Draft D4 Scope – some of which have recognized deficiencies, as discussed above – the agency has not specified how it plans to assess the applicability, appropriateness, and uncertainty of such models. In the final D4 scope, the agency must outline the criteria used for model selection, as well as the specific steps it intends to take to characterize uncertainty around any modeled estimates whether as inputs to models or estimates from models. Robust uncertainty analyses are necessary for describing the level of confidence associated with modeled variables relied upon to characterize D4 risk and to support distributional characterizations of risk.

In past reviews of draft risk evaluations, the SACC has urged EPA to better document uncertainties and assumptions associated with exposure model inputs, specifying that the agency should employ sensitivity analyses to assess how gaps in the exposure assessments affect the risk estimates.^{58,59} Other approaches to quantitative analysis of uncertainty – such as analytical uncertainty propagation, probabilistic uncertainty analysis, and classical statistical methods – are outlined in the *Exposure Factors Handbook* developed by EPA’s Office of Research and Development (ORD).⁶⁰ We suggest that EPA reference this Handbook as it determines the specific steps it will take to assess uncertainty.

In short, in the final scope for D4, EPA should update its analysis plan to explicitly reflect how it plans to (1) select appropriate exposure models and (2) analyze and characterize uncertainty associated with the various models used.

B. EPA must conduct uncertainty analysis when relying on chemical analogs.

The Draft D4 Scope analysis plan indicates that whenever EPA lacks release, hazard, or exposure data on a chemical – rather than requiring the missing information to be submitted or developed, EPA will use information it has on so-called “analog” or “surrogate” chemicals. In fact, EPA explicitly states that it “plans to augment and/or supplement data through the use of models and potential surrogate data where appropriate” (Draft D4 Scope, p. 48) such as to fill

⁵⁸ U.S. EPA. (2020, August). *Summary of External Peer Review and Public Comments and Disposition for 1-Bromopropane (n-Propyl Bromide)*, p. 97.
https://www.epa.gov/sites/default/files/2020-08/documents/summary_of_external_peer_review_and_public_comments_and_disposition_for_1-bromopropane_n-propyl_bromide.pdf

⁵⁹ U.S. EPA. (2020, June). *Summary of External Peer Review and Public Comments and Disposition for Methylene Chloride (MC)*, p. 23 and 30.
https://www.epa.gov/sites/default/files/2020-06/documents/2_mecl_peer_review_and_public_comment_response_final.pdf

⁶⁰ U.S. EPA (2011, September). *Exposure Factors Handbook*.
<https://www.nrc.gov/docs/ML1400/ML14007A666.pdf>

gaps around environmental releases (Draft D4 Scope, p. 48) and occupational exposures (Draft D4 Scope, p. 51).

Notably absent from the analysis plan, however, is any acknowledgment of the uncertainty associated with relying on surrogate data or how EPA will identify and account for that uncertainty. Here, as in other settings where EPA heavily relies on surrogate data, such as in EPA's new chemicals program,⁶¹ the agency has failed to identify and adopt any quantitative metric for measuring the accuracy of an analog or surrogate chemical, or any description, let alone analysis, of the degree of confidence to be placed in its selection of such chemicals to represent the chemical being evaluated.

As we have repeatedly indicated in these comments, EPA should be making much greater use of its information authorities to fill information gaps and do so immediately. However, to the extent EPA does rely on surrogate data, EPA will need to conduct robust uncertainty analyses. ORD has an existing method of assessing analogs.^{62, 63} EPA should consider adopting ORD's approach and specify the adoption of this approach, or any other relevant approaches, in the final D4 scope.

11. EPA cannot ignore a release of or exposure to a chemical on the basis that it cannot attribute it to a particular condition of use in its analysis plan.

Similar to past risk evaluation scopes, EPA makes several statements in the Draft D4 Scope indicating its intent to attribute chemical releases and exposures to a particular condition of use, such as plans to:

- “[m]ap or group each condition of use to a release assessment scenario(s)” (p. 49),
- “[g]roup each condition(s) of use to environmental assessment scenarios” (p.50),

⁶¹ In contrast to the new chemicals setting, where EPA has only very limited time to conduct its reviews, for existing chemicals that must go through a multi-year process of prioritization scoping, and risk evaluation, Congress gave EPA ample time – if it would only utilize it – to require the submission or development of needed information. Yet EPA has steadfastly refused to do so.

⁶² Lambert, J.C. (2019, May 2-3). *U.S. EPA's Use of Read-Across in Provisional Peer-Reviewed Toxicity Value Assessments*. [Presented at Office of Environmental Health Hazard Assessment (OEHHA) of Cal EPA Workshop on Read-Across, Oakland, CA]. Retrieved October 25, 2021 from <https://doi.org/10.23645/epacomptox.8126810>

⁶³ U.S. EPA (2021, August 19). *Basic Information About Provisional Peer-Reviewed Toxicity Values (PPRTVs)*. [See Item 5, “What is an expert-driven read across approach?”]. Retrieved October 25, 2021 from <https://www.epa.gov/pprtv/basic-information-about-provisional-peer-reviewed-toxicity-values-pprtvs>

- “[m]ap or group each condition of use to occupational exposure assessment scenario(s)” (p. 52),
- “[g]roup each condition of use to consumer exposure assessment scenario(s)” (p. 53); and finally,
- “[m]ap or group each condition of use to general population exposure assessment scenario(s)” (p. 55).

Unfortunately, EPA does not provide an explanation for implementing this approach, which leaves the public with little information on the need for or effectiveness of such an approach. EPA’s repeated language around “grouping” conditions of use to exposure scenarios suggests EPA believes it must be able to attribute every release of a chemical to a particular condition of use in order to consider its risks in a risk evaluation. This is not the case.

Nothing in TSCA allows EPA to ignore data simply because they have not been tied to a particular condition of use. EPA must conduct risk evaluations under TSCA that consider all “reasonably available” information relating to a chemical substance, including information that may not be tied to specific conditions of use.⁶⁴ EPA’s rules further define “reasonably available information” as “information that EPA possesses or can reasonably generate, obtain and synthesize for use”⁶⁵

Data that cannot be attributed to specific conditions of use are still relevant to determining whether *the chemical substance* presents an unreasonable risk, and as such must be considered by EPA. As an example, EPA may have biomonitoring data that indicate people are exposed to a chemical at quantifiable levels. EPA cannot ignore such data simply because it has not determined, or even cannot determine, how much of the exposure is attributable to a particular condition of use. Such a consideration may be more relevant at any subsequent risk management stage when EPA may need to understand the extent to which specific measures will reduce exposure and risk; but that future need provides no basis for EPA to ignore risk-relevant information at the risk evaluation stage.

12. EPA should evaluate combined exposures to all relevant receptors.

EDF is encouraged by EPA’s plans to “[r]efine and finalize exposure scenarios for general population by considering combinations of sources and uses, exposure pathways including routes, and exposed populations” (p. 54), as well as to consider combinations of exposures for

⁶⁴ TSCA Section 26(k)

⁶⁵ 40 C.F.R. §§ 702.3, 702.33

consumers (p. 53). However, this language in the Draft D4 Scope is similar to that of previous draft scopes, raising concerns that EPA may inadequately or incompletely evaluate combined exposures to D4. With some exceptions, previous draft scopes were largely silent on whether EPA planned to assess combined exposures in its risk evaluations, and the final risk evaluations for some of the first ten chemicals failed to properly assess combined exposures. In the final D4 scope, EPA should indicate affirmatively that it will assess combined exposures to *all relevant receptors*.

It seems EPA is not planning to look at combined exposures to all relevant receptors, as there is no mention of assessing aggregate or combined exposures for occupational uses. EPA's decision to ignore combined worker exposures not only ignores workers as a potentially exposed or susceptible subpopulation, but also fails to meet the standards of TSCA Section 6(a).

TSCA's provisions direct EPA to prepare risk evaluations and the related findings for "chemical substances" as a whole, not for specific or limited hazards, exposures, or conditions of use of those substances. For example, the risk management provision at TSCA Section 6(a) expressly requires EPA to address risks when the risks arise from combined sources of exposure: "If [EPA] determines in accordance with [the risk evaluation provision] that the manufacture, processing, distribution in commerce, use, or disposal of a chemical substance or mixture, or that *any combination of such activities*, presents an unreasonable risk of injury to health or the environment," then EPA must issue a risk management rule.⁶⁶ Thus, if exposures resulting from "any combination" of conditions of use present an unreasonable risk, EPA must issue a risk management rule. But EPA must analyze *all* of the exposures resulting from these activities to assess whether *any combination* presents such a risk.

Based on the information shown in the conceptual models (Draft D4 Scope, Appendices F-H), there are numerous ways in which individuals or groups are known or reasonably foreseen to experience exposures to D4 from multiple conditions of use and exposure pathways. In finalizing the D4 scope, EPA needs to indicate that it will examine combined exposures to all relevant receptors – including workers.

13. EPA should include relevant co-exposures in the final D4 scope.

While EPA refers to potentially evaluating background exposures to D4 in the Draft D4 Scope (Section 2.2.2), the agency makes no indication that it will consider co-exposures to other relevant chemical and non-chemical stressors. TSCA plainly authorizes, and arguably mandates, that the agency take a cumulative approach to evaluating chemical risks given the statute's requirements to use the best available science and to protect potentially exposed or susceptible subpopulations.

⁶⁶ TSCA Section 6(a) (emphasis added); *see also* TSCA Section 9(a) (using same language in provision governing requests to other federal agencies to address risks).

As with background exposures to D4, comprehensively evaluating potential chemical risk in accordance with best available science demands considering not only the totality of exposure to D4 via TSCA and non-TSCA conditions of use (e.g., food and food packaging, personal care products, and medical applications), but also considering co-exposures to stressors that present similar hazards to D4 and therefore bear on the extent to which D4 presents risk. Such consideration is necessary to the evaluation and management of risk to certain subpopulations who are more susceptible to the effects of D4 by virtue of co-exposures to other substances that present similar health effects.

The 2008 National Research Council (NRC) report, *Phthalates and Cumulative Risk Assessment: The Tasks Ahead* (NRC 2008 Report), broadly recommends evaluating chemical substances using a cumulative risk assessment approach. In the report, the NRC notes:

[The] committee concludes that it is plausible and warranted to extend cumulative risk assessment to include chemicals associated with common adverse outcomes as exemplified in this report by inclusion of other antiandrogenic chemicals with phthalates. To cite another example, EPA could evaluate combined exposures to lead, methylmercury, and polychlorinated biphenyls because all contribute to cumulative risk of cognitive deficits consistent with IQ reduction in children, although the deficits are produced by different mechanisms of action. Cumulative risk assessment based on common adverse outcomes is a feasible and physiologically relevant approach to the evaluation of the multiplicity of human exposures and directly reflects EPA's mission to protect human health.

Unfortunately, EPA has indicated elsewhere that EPA is prohibited from considering co-exposures to other chemical and non-chemical stressors in manufacturer-requested chemical risk evaluations. Specifically, in response to public comments on the Draft Scopes for DIDP and DINP, EPA stated:

Two separate manufacturer requests for evaluation were made specifically for DIDP (CASRN 26761-40-0 and 68515-49-1) and for DINP (CASRNs 28553-12-0 and 68515-48-0) and not for other chemicals or other phthalates. Since EPA's authority to conduct a manufacturer-requested risk evaluation is tied to the "chemical substance [or category of chemical substances]...that a manufacturer of the chemical substance has requested...be subjected to a risk evaluation," (TSCA section 6(b)(4)(C)) EPA cannot add additional phthalates to the scope of the risk evaluations for DIDP and DINP, as doing so would go beyond the scope of the risk evaluation.

EDF wholeheartedly disagrees with EPA's reading of the referenced provisions, and notes that adopting EPA's interpretation would effectively establish a scientific and regulatory double standard for risk evaluations of chemicals that are initiated through the prioritization process versus through the manufacturer-requested process. Among other issues, that is logically

untenable. As indicated earlier, TSCA requires consideration of relevant co-exposures. We recommend that the final D4 scope include consideration of relevant co-exposures, and that EPA augment its information search and inclusion strategies accordingly

14. EPA does not provide detail on how the agency plans to solicit and incorporate population-specific exposure factors.

In the Draft D4 Scope, EPA says it “plans to consider whether [consumer] exposures for adults may differ from those of children due to different activities (e.g., children may mouth certain products) or exposure factors (e.g., inhalation rates).” (p. 54) The agency also “plans to consider age-specific behaviors, activity patterns, and exposure factors unique to any [potentially exposed or susceptible subpopulations] for [general population] exposure scenarios that involve those subpopulations (e.g., children may have different intake rates for soil than adults; infants may be exposed via ingestion of human milk).” (p. 56)

We applaud EPA’s efforts to account for population-specific exposure factors in its consumer and general population exposure analysis plan. However, it is unclear how EPA intends to gather information on “age-specific behaviors, activity patterns, and exposure factors.” The final D4 scope should describe the agency’s approach to determining population-specific exposure factors.

We recommend the agency take the following multi-faceted approach:

- EPA should use its information authorities to fill identified data gaps regarding population-specific exposure factors (e.g., exposure factors relevant to fenceline communities as discussed in Section 8).
- EPA should take advantage, as appropriate, of publicly available sources such as the National Health and Nutrition Examination Survey (NHANES) to ascertain where there may be differential exposures across different demographic characteristics, and internal resources such as the CompTox chemicals dashboard that includes information regarding chemical product and use categories and exposure predictions.^{67, 68}
- EPA should obtain information directly from identified potentially exposed or susceptible subpopulations. For example, EPA should seek information directly from fenceline communities and other EJ groups, as early as possible. There is an opportunity to implement this approach by expanding EPA’s EJ and Tribal consultations under TSCA.

⁶⁷ U.S. CDC. (n.d.). *National Health and Nutrition Examination Survey: 1999–2020 Survey Content Brochure*. Retrieved October 25, 2021 from https://wwwn.cdc.gov/nchs/data/nhanes/survey_contents.pdf

⁶⁸ U.S. EPA. (n.d.). *CompTox Chemicals Dashboard*. Retrieved October 25, 2021 from <https://comptox.epa.gov/dashboard>

EPA should hold EJ and Tribal community consultations for the D4 risk evaluation starting *now, at the scoping stage*.

15. EPA must evaluate the potential for D4 cancer hazard and risk if there is evidence of potential carcinogenicity.

In the Draft Hazard Analysis Plan for D4, EPA has included a statement that reads:

The cancer mode of action (MOA) analyses determine the relevancy of animal data to human risk and how data can be quantitatively evaluated. If the D4 cancer hazard is determined to be relevant to humans (emphasis added), EPA plans to evaluate information on genotoxicity and the mode of action for all cancer endpoints to determine the appropriate approach for quantitative cancer assessment in accordance with the U.S. EPA Guidelines for Carcinogen Risk Assessment (U.S. EPA, 2005b). (Draft D4 Scope, p. 58)

EDF finds this statement both unclear and problematic. EPA seems to suggest that it will rely on mode of action (MOA) to determine the relevancy of animal data to humans. We advise EPA to proceed with extreme caution, as this approach assumes that a definitive D4 MOA for cancer is known, and that available toxicological data is sufficient to capture any other potential mechanisms of action for cancer in humans. Unless there is strong empirical evidence that D4 only operates through a single, particular MOA with respect to cancer *and* that mode of action is irrelevant to humans, we recommend EPA use animal toxicological data to characterize D4 cancer risk to humans.

Separately, the excerpt above presents a circular logic. EPA indicates that it plans to determine the “relevancy” of animal data by analyzing MOA, but then EPA goes on to say that the agency will only evaluate information on “genotoxicity *and the MOA* (emphasis added)” if animal data is deemed relevant. These statements are contradictory.

If there is any evidence of carcinogenicity, then it is entirely relevant to characterizing potential cancer risk to humans, and the final D4 scope should be revised to include cancer as an endpoint.

16. EPA should employ a unified framework for dose-response assessment of cancer and non-cancer endpoints.

EPA indicates in the Human Health Hazards section of the Draft D4 Scope that it will use different approaches for cancer and non-cancer endpoints:

Dose-response assessment will be performed in accordance with EPA guidance (U.S. EPA, 2012a, 2011b, 1994) developing points of departure (POD) for either margins of exposure (MOEs), cancer slope factors (CSFs), oral slope factors (OSFs), and/or inhalation unit risks (IURs). Dose-response analyses may be used

if the data meet data quality criteria and if additional information on the identified hazard endpoints are not reasonably available or would not alter the analysis. (p. 58)

As expressed in multiple past comments addressing EPA's assessment of chemicals, EDF strongly recommends that EPA move toward a unified approach for dose-response assessment of cancer and non-cancer effects. This approach was recommended by the National Academies in its seminal report, *Science and Decisions: Advancing Risk Assessment*:

Scientific and risk-management considerations both support unification of cancer and noncancer dose-response assessment approaches. The committee therefore recommends a consistent, unified approach for dose-response modeling that includes formal, systematic assessment of background disease processes and exposures, possible vulnerable populations, and modes of action that may affect a chemical's dose-response relationship in humans.⁶⁹

EPA should describe its efforts to adopt a unified approach to dose-response assessment of cancer and non-cancer endpoints in the final D4 scope.

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EDF appreciates the opportunity to provide comments and EPA's consideration of them.

⁶⁹ National Research Council. (2009). *Science and Decisions: Advancing Risk Assessment*. Washington, DC: *The National Academies Press*, p. 9. <https://doi.org/10.17226/12209>