United States
Environmental Protection Agency

Office of Chemical Safety and
Pollution Prevention
February 2022

EPA Response to Public Comments Received on the Draft Scope of the Risk Evaluation under the Toxic Substances Control Act (TSCA) for:

Octamethylcyclotetra- siloxane (Cyclotetrasiloxane, 2,2,4,4,6,6,8,8-octamethyl-)

(D4)

CASRN 556-67-2

February 2022

Summary of Public Comments Received on the Draft Scope of the Risk Evaluations for Octamethylcyclotetra- siloxane (D4) under the Toxic Substances Control Act (TSCA)

In this document, the U.S. Environmental Protection Agency (EPA) is responding to comments received during the public comment period following announcement of the draft scope of the risk evaluation under the Toxic Substances Control Act (TSCA) to be conducted for octamethylcyclotetra- siloxane **(**D4) (CASRN 556-67-2), a chemical substance for which EPA received a manufacturer request for risk evaluation (MRRE) on March 19, 2020.

Comments were received during a 45-day public comment period following the announcement of the draft scope document for D4 under TSCA (86 FR 50347 [September 8, 2021]). During the comment period, the public was invited to submit comments on EPA's draft scope document, including additional data or information relevant to the chemical substances or that otherwise could be useful to the Agency in finalizing the scope of the risk evaluation. To the extent that comments provided information on conditions of use, as well as other elements of the draft scope document, those comments and other submitted information (*e.g.*, relevant studies and assessments) were used to inform revisions to the draft scope document and may be considered in subsequent phases of the risk evaluation process.

EPA received six comment submissions from six different entities, including three potentially affected businesses or trade associations, one private individual, one environmental advocacy group, and one group of academics, scientists, and clinicians. The table below presents the commenters and corresponding docket submission numbers.

Comments addressed the overall risk evaluation process (*e.g.*, the overall approach to the scope documents and risk evaluation process, including collection, consideration, and systematic review of relevant information); the specific elements of the scope documents (*e.g.*, hazard, exposure, potentially exposed or susceptible subpopulations [PESS]); and information specific to the D4 (*e.g.*, relevant studies, assessments, degradation products, conditions of use).

Commenter Name/Organization	Docket Number
John Tranquilli	EPA-HQ-OPPT-2018-0443-0026
Eastman Chemical Company	EPA-HQ-OPPT-2018-0443-0027
Silicones Environmental, Health, and Safety Center (SEHSC)	EPA-HQ-OPPT-2018-0443-0028
University of California, San Francisco (UCSF) Program on Reproductive Health and the Environment (PRHE) and affiliates	EPA-HQ-OPPT-2018-0443-0029
Environmental Defense Fund	EPA-HQ-OPPT-2018-0443-0030
Alliance for Automotive Innovation	EPA-HQ-OPPT-2018-0443-0031

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1 OVERALL RISK EVALUATION PROCESS

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0028) requested that EPA clarify which specific federal agencies, if any, reviewed and commented on the draft scope document. The commenter also requested that EPA describe the anticipated role, if any, and the process for agencies to participate in the preparation and review of the D4 risk evaluation, including the timing for making input received from other federal agencies available in the docket for public review.

Response: Feedback was requested from interagency partners including, but not limited to, the Consumer Product Safety Commission (CPSC), National Institute for Occupational Safety and Health (NIOSH), the Occupational Safety and Health Administration (OSHA), Small Business Administration (SBA), and the Department of Defense (DOD). One comment was received from DOD about a mission critical use (see EPA-HQ-OPPT-2018-0443-0032). EPA expects to gain additional information from interagency reviewers about any mission critical uses and exposure scenarios during the development of the draft risk evaluation and intends to make relevant information available in the public docket when the draft risk evaluation is published for public review.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0028) identified six elements specified in the Risk Evaluation Rule (82 FR 33726 (July 20, 2017)) that they claimed merit attention to help ensure that the MRRE for D4 will fully satisfy the requirements of the Agency's Risk Evaluation Rule and TSCA.

Response: The Agency believes that the final scope of the risk evaluation for D4 fully satisfies the relevant requirements of TSCA and notes that the scope provides specific information on how the Agency fulfilled elements required by TSCA section 6(b)(4)(D) and 40 CFR 702.41. In accordance with 40 CFR 702.41(c), the draft scope document and final scope document include the following information: the conditions of use that EPA plans to consider during risk evaluation; the PESS, hazards and exposures that EPA plans to evaluate; a description of the reasonably available information and science approaches EPA plans to use; and a conceptual model, analysis plan, and plan for peer review for each category of chemical substances.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0028) noted that they had previously expressed concerns to EPA regarding delays in the processing of D4 MRRE, pointing out that the draft scope is only the first step in the risk evaluation process and that the Agency is already over 6 months behind the schedule mandated by TSCA and EPA's Risk Evaluation Rule (82 FR 33726 (July 20, 2017)). The commenter expressed that they are committed to working with the Agency to facilitate the timely completion of the D4 risk evaluation.

Response: EPA thanks SEHSC and its members for their commitment to working with the Agency to help ensure the timely completion of the D4 risk evaluation.

1.1 Approach to Scope Documents

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0028) requested that the Agency describe its plan for peer review beyond citing generally to guidance documents and TSCA (*e.g.,* who will conduct the peer review, what methods will be used, when will the peer review occur, etc.) and how that process will fit within the timing mandates of TSCA and the Risk Evaluation Rule (82 FR 33726, 33744; July 20, 2017).

Response: The 2017 Final Risk Evaluation Rule does not identify who must conduct the peer reviews for the risk evaluations, just that they must be done and be consistent with Agency and Office of Management and Budget guidance with respect to peer review processes.

Related Comments:

- One commenter (EPA-HQ-OPPT-2018-0443-0029) expressed concern that the draft analysis plan (Section 2.7 of the draft scope document) lacked important details and is "extremely vague," citing EPA's Human Health Risk Assessment Framework as a comparison. The commenter notes that EPA has enough experience with TSCA risk evaluations so as to be able to provide more detail in the analysis plan regarding approaches and outputs that can be expected in the risk evaluation. Additional details would make the scope document more useful for EPA, more informative to the public and provide EPA the opportunity to make any necessary revisions to its approach based on public comment before it completes a draft risk evaluation that will then be peer reviewed and subject to public comment.

- The same commenter (EPA-HQ-OPPT-2018-0443-0029) asserted that the consumer exposure section of the draft analysis plan (Section 2.7.2.4) does not provide basic information about the planned assessment, such as routes of exposure, exposure duration, or approach to accounting for variability in exposure due to factors such as consumer product formulation, usage pattern (*e.g.*, amount, duration, and frequency of use), or exposure environment (*e.g.*, air exchange rate). The final element of the consumer exposures section of the analysis plan is to "Evaluate the weight of the scientific evidence of consumer exposure estimates based on different approaches." The plan should explain the objective of this weight of the scientific evidence evaluation and its intended output. The commenter inquired about what parameters are to be estimated; in what units/metrics they are expressed; whether each value is intended to be a "best estimate"; and whether there is any accounting for uncertainty and variability in the parameter values?

- The same commenter (EPA-HQ-OPPT-2018-0443-0029) recommended that the final element of the general population draft analysis plan should explain the objective of this weight of the scientific evidence evaluation and its intended output. The commenter inquired about what parameters are to be estimated; in what units/metrics are they expressed; whether each value is intended to be a "best estimate"; and whether there is any accounting for uncertainty and variability in the parameter values?

- The same commenter (EPA-HQ-OPPT-2018-0443-0029) asserted that the expected contents of the first tier analyses in the general population section of the draft analysis plan (Section 2.7.2.5) are unclear, and no indication is provided of how their results will inform a decision regarding whether more refined analysis will be conducted, or whether variability in exposure and susceptibility across PESS will be considered in that decision.

- The same commenter (EPA-HQ-OPPT-2018-0443-0029) asserted that the environmental releases section of the draft analysis plan (Section 2.7.2.2 of the draft scope document) should explain the objective of the weight of the scientific evidence evaluation and its intended output. The commenter identified information that would be good to include, such as the parameters to be estimated, the units/metrics they are expressed in, whether each value is intended to be a "best estimate," and whether there is any accounting for uncertainty and variability in the parameter values?

- The same commenter (EPA-HQ-OPPT-2018-0443-0029) requested that EPA provide clarification in Section 2.7.2.1 of the draft analysis plan in the draft scope document by explaining the objective of this weight of the scientific evidence evaluation and its intended output, specifically what parameters are to be estimated, in what units/metrics they are expressed, whether each value is intended to be a "best estimate," and whether there is any accounting for uncertainty and variability in the parameter values?

Response: The purpose of the scope document is to develop clear objectives to support a quantitative risk analysis for the assessment as well as to define the steps that EPA plans to take in conducting different components of the risk evaluation. It also helps to guide the systematic review approach and/or methods that will be used to identify, evaluate, analyze, and integrate evidence. Following publication of the D4 final scope, EPA will conduct the data evaluation and integration phases of systematic review. The draft risk evaluation for D4 will include more detailed descriptions of specific analytical methods and how different data were used to inform the assessment. There will be opportunities to provide input during the public comment period for the draft D4 risk evaluation.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0030) asserted EPA must conduct uncertainty analysis when relying on chemical analogs and that the Agency failed to (1) identify and adopt any quantitative metric for measuring the accuracy of an analog or surrogate chemical, or (2) provide any description and analysis of the degree of confidence. The commenter pointed out that EPA's Office of Research and Development (ORD) has an existing method of assessing analogs and recommended EPA consider adopting ORD's approach and specify the adoption of this approach, or any other relevant approaches, in the final D4 scope.

Response: During the risk evaluation process, EPA will determine whether to use analogs or surrogate chemicals and will provide a description of the methods used to determine the suitability of any analog and the information associated with the analog. The Office of Pollution Prevention and Toxics (OPPT) will consult with other Agency programs and offices where appropriate.

1.2 Potentially Exposed or Susceptible Subpopulations

Related Comments:

- One commenter (EPA-HQ-OPPT-2018-0443-0029) asserted that EPA must address PESS more robustly to adequately consider exposure risks, citing scientific evidence demonstrating that intrinsic and extrinsic factors can change exposures and susceptibility to environmental chemical exposure risks. The commenter identified intrinsic factors such as physiological parameters specific to life stage that may make individuals more or less vulnerable to environmental exposures. The commenter provided the example of young infants (less than 3 months old) who have lower lipid content with respect to adults (reducing their relative retention of lipophilic chemicals) while older infants have higher lipid content with respect to adults (increasing their relative retention of lipophilic chemicals). The commenter also described extrinsic factors—including social stressors, lack of access to health care facilities, healthy food, health information, and adequate formal education opportunities for health literacy—that can compound the negative effects of environmental exposures among these subpopulations.

- The same commenter (EPA-HQ-OPPT-2018-0443-0029) agreed with the inclusion of the PESS groups identified by EPA in the draft scope document but claimed that the list of PESS fails to account for individuals with chronic conditions and people who live or work near manufacturing, processing, use, or disposal sites.

- In an additional comment, the same commenter (EPA-HQ-OPPT-2018-0443-0029) recommended that the EPA explicitly adopt an expanded definition of PESS that highlights the role of intrinsic and extrinsic factors that influence susceptibility. This would complement EPA's plans to "increase consideration of environmental justice issues."

- Another commenter (EPA-HQ-OPPT-2018-0443-0030) asserted that the identification of subpopulations is not comprehensive and that EPA should identify specific PESS, including but not limited to, fenceline communities. The commenter noted that while EPA does discuss performing "fenceline analysis where appropriate to screen for potential effects with emphasis on PESS and environmental justice communities," they are concerned about the Agency's non-committal language. The commenter recommends EPA assess all relevant fenceline communities and consider all studies regarding PESS as primary evidence, regardless of whether they provide information about health outcomes, and not as supplemental information.

- Another commenter (EPA-HQ-OPPT-2018-0443-0028) urged EPA to describe more fully and provide opportunity for commenting on the methodology and data to be used for performing the "fenceline analyses" referenced on pages 40 and 55 of the draft scope for D4 to screen for potential effects on the general population, PESS, and environmental justice communities, as well as the processes for conducting an in-depth analysis, where warranted.

Response: EPA will detail the PESS considered in the draft risk evaluation after completing its full evaluation, synthesis, and integration of the exposure literature. EPA plans to identify PESS based on intrinsic and extrinsic factors presented in reasonably available information. Some of the PESS that EPA plans to consider include children, women of reproductive age, workers, occupational non-users (ONUs), consumers, and bystanders. Additionally, EPA plans to analyze all reasonably available information in order to determine whether some human receptor groups might be exposed via exposure pathways that could be distinct to a particular subpopulation or life stage; for example, women of reproductive age who may be or become pregnant; lactating women; infants, toddlers, children at various developmental stages in life; and elderly. EPA also plans to consider whether some human receptor groups may have higher exposure via identified pathways due to unique characteristics (e.g., activities, duration, location of exposure) when compared with the general population. Likewise, EPA plans to evaluate reasonably available human health hazard information to determine whether some human receptor groups might have greater susceptibility than the general population to the chemical's hazard(s).

EPA acknowledges that exposures (and any subsequent risk) may vary due to differences among individuals, populations, spatial and temporal scales, and other factors. When building exposure scenarios for identified conditions of use for D4, EPA plans to consider the spatial and temporal relevance of reasonably available information, including information regarding chemical emissions. For example, communities living near identified sources of emissions from manufacturing, processing, use, or disposal may experience greater exposure than the general population. EPA cannot provide details on its fenceline analyses before systematic review of all reasonable available information is completed. The draft risk evaluation for D4 will include more detailed descriptions of specific analytical methods and how different data were used to inform the assessment. There will be opportunities to comment during the public comment period for the draft D4 risk evaluation.

Related Comments:

- One commenter (EPA-HQ-OPPT-2018-0443-0029) recommended that because D4 is used in personal care products, EPA should consider differences in use by race/ethnicity given that

previous research finds that certain populations can have higher exposures via personal care products. These individuals must also be considered PESS.

- The same commenter (EPA-HQ-OPPT-2018-0443-0029) observed that Section 2.7.2.5 of the draft scope does not include identification of the characteristics (*e.g.*, race/ethnicity, income, lifestage) of populations living in proximity to facilities releasing D4 to the environment, which is necessary information to assess risks to PESS.

Response: Many personal care products are drugs, cosmetics, or devices that are excluded from the TSCA definition of "chemical substances" (see TSCA section 3(2)). Exposure to these products could be part of an aggregate exposure analysis if deemed appropriate for the particular scenario and will be determined during risk evaluation. EPA plans to include and address environmental justice considerations by (1) evaluating reasonably available information on factors such as unique pathways, cumulative exposure from multiple stressors, and behavioral, biological, or environmental factors that increase susceptibility; (2) identifying unique considerations for subsistence populations when relevant; and (3) following best practices from EPA's Technical Guidance for Assessing Environmental Justice in Regulatory Analysis (U.S. EPA, 2016).

1.3 Aggregate and Cumulative Exposure

Related Comments:

- One commenter (EPA-HQ-OPPT-2018-0443-0029) asserted that EPA must account for the combined exposures and risks from multiple roles related to the conditions of use; for example, a woman of reproductive age who works in the production of D4; uses consumer products containing D4; and lives near a manufacturing, processing, distribution, use, or disposal site for D4. The commenter also noted that analyzing the impact of compounding factors is critical to understanding the health risks of exposure when considering D4. The commenter recommended that EPA incorporate aggregate exposure scenarios where some individuals may be exposed to D4 through combinations of occupational, consumer, and general population settings when considering all routes of exposure scenarios for conditions of use. The commenter also asserted that EPA should consider cumulative risk assessment. Lastly, the commenter recommended that EPA account for exposure to multiple related stressors (*e.g.*, considering chemical classes and mixtures rather than a chemical-by-chemical approach, evaluating cumulative exposure to non-chemical stressors). Aggregate exposure should also include, according to the commenter, all pathways and routes of human exposure (*i.e.*, dermal, oral, and inhalation routes), asserting that if EPA ignores any exposure scenarios or does not fully combine all possible sources, pathways, and routes of exposures (including the non-TSCA uses described above), then the Agency will underestimate human health risks of D4, including for PESS.

- Another commenter (EPA-HQ-OPPT-2018-0443-0030) emphasized that there is no mention of assessing aggregate or combined exposures for occupational uses. The commenter asserted this decision not only ignores workers as a PESS, but also fails to meet the standards of TSCA section 6(a). The commenter noted that based on the information shown in the conceptual models (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. The commenter recommended that EPA state whether it will examine combined exposures to all relevant receptors, including workers, in the final scope for D4.

Response: EPA has not ruled out combined exposures or aggregate analysis. EPA defines aggregate exposures as the combined exposures to an individual from a single chemical substance across multiple

routes (i.e., dermal, inhalation, or oral) and pathways (i.e., exposure from different sources) at 40 CFR 702.33. EPA recognizes that a worker may be exposed via multiple routes at the workplace and that additional exposure can occur from being in the general population and using consumer products after leaving the facility. Furthermore, EPA acknowledges that consumers and the general population may also be exposed to D4 via multiple routes. For all groups, these exposures may be additive across routes, pathways, receptors, and chemical stressors. The magnitude, frequency, and duration of exposures and the associated routes of exposure will depend upon the conditions of use.

Exposure scenarios will be developed based on the reasonably available information, weight of the scientific evidence, and fit-for-purpose approaches. EPA will determine whether to consider aggregate exposure assessment for D4 after evaluating all reasonably available information during systematic review.

EPA is currently considering cumulative exposures and risks from high-priority substances that have similar modes of action (MOA) in human organ systems. The most prominent aspect of cumulative risk assessment is often the prediction of the combined effects of multiple stressors. In circumstances where EPA determines it is appropriate to conduct a cumulative risk assessment for a particular chemical substance—during the synthesis and evidence integration phases—EPA will both integrate the hazard and dose-response relevant to the stressor(s) of interest. The Agency will also perform an analysis of exposure(s) to those stressor(s), including reviewing information related to the integration of exposure, hazard, and dose-response information that could be applicable to a cumulative risk assessment. These include multiple-stressor hazard, dose-response and exposure issues, exposure time or duration-related issues, susceptibility of the study population along with the influencing factors (including life stage), and subpopulations with special exposures.

Related Comments:

- One commenter (EPA-HQ-OPPT-2018-0443-0030) stated that evaluating D4's potential risk demands considering not only the totality of exposure via TSCA and non-TSCA conditions of use, but also co-exposures to stressors that present similar hazards. The commenter asserted that EPA's statement in the *EPA Response to Public Comments Received on the Draft Scopes of the Risk Evaluations Under the Toxic Substances Control Act (TSCA) for: Di-isodecyl Phthalate (DIDP) (1,2-Benzenedicarboxylic acid, 1,2-diisodecyl ester and 1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich) CASRN 26761-40-0 and 68515-49-1* (EPA-HQ-OPPT-2018-0436-0038) that the Agency is prohibited from considering co-exposures to other chemical and non-chemical stressors in MRREs would effectively establish a double standard for risk evaluations that are initiated through the prioritization process versus through the manufacturer-requested process. The commenter stated that TSCA also requires consideration of relevant co-exposures and urges EPA to include relevant co-exposures and revisions to the information search and inclusion strategies in the D4 final scope.

- Another commenter (EPA-HQ-OPPT-2018-0443-0029) asserted that EPA must consider every exposure scenario and fully aggregate all possible sources, pathways, and routes of exposures (including non-TSCA uses), to accurately estimate human health risks of D4, including for PESS. The commenter stated that the comprehensive evaluation of release scenarios is important and should be accompanied by aggregation of all potential sources of exposures across each condition of use, including non-TSCA uses of D4 in order to fully assess potential health risks.

Response: A request for MRRE was submitted specifically for D4 and not for other chemical substances. Because EPA's authority to conduct an MRRE 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)), the Agency cannot add additional co-exposures to other chemical substances to the scope of the risk evaluations for D4, as doing so would go beyond the scope of the MRRE. Under TSCA section 6(b)(4)(F), EPA is not required to conduct cumulative risk evaluations; rather, EPA must describe whether aggregate or sentinel exposure were considered as well as the basis for that consideration.

As stated in Section 2.2.2 of the scope document, although EPA would not regulate non-TSCA uses, consideration of 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 (e.g., as background exposures that would be accounted for should EPA decide to evaluate aggregate exposures). The Agency will determine during the risk evaluation whether to conduct and what information would be needed for any background or aggregate analyses.

1.4 Physical and Chemical Properties and Fate Endpoints

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0028) stated that based on the vapor pressure of D4 at room temperature, it is inappropriate to describe D4 as oily. The commenter recommended to avoid using this term in future descriptions and instead reference specific physical and chemical characteristic (*e.g.*, immiscible liquid).

Response: The available high quality references describe D4 as an oily liquid or smooth, viscous liquid. EPA now refers to D4 as a "smooth, viscous liquid" in the final scope document.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0029) asserted that the studies that EPA is using to understand D4's persistence in the environment are not accurately approximating real-world values and thus do not represent the "best available science."

Response: EPA conducted a comprehensive search for reasonably available information to support the development of the draft scope document for D4. EPA leveraged the data and information sources already identified in the SEHSC submission requesting that the Agency conduct the risk evaluation for D4. The values for the environmental fate properties may be updated as EPA evaluates and integrates additional information into the risk evaluation through systematic review methods and information provided during the public comment period for the draft scope.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0029) noted that reported measurements of the K_{OC} of D4 in the literature can vary by over half a log unit, which has important implications for calculations of environmental fate and persistence. The commenter expressed concern that different conclusions could be drawn, depending on which set of values is used. The commenter gave the example of modeled residence time, stating that values for D4 may differ by over 100 days and may or may not exceed regulatory thresholds for persistence, making the choice of physical and chemical properties critical for the D4 risk evaluation.

Response: Appendix C of the draft scope listed several measured and calculated values for the organic carbon: water partitioning coefficient (K_{OC}) of D4. Measured data and, where necessary, model predictions of physical and chemical properties and environmental fate endpoints will be used to characterize the persistence and movement of D4 within and across environmental media.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0029) asserted that Section 2.7.1 of the draft D4 scope document failed to identify the physical and chemical properties for which measured or

modeled values are needed; the commenter asked whether this information is found elsewhere in the scope document, and if so, it should be referenced in this section for clarity. The draft scope also indicates that a "a weight of the scientific evidence evaluation of physical and chemical properties and environmental fate data" will be conducted but does not state the objective of evaluation and its intended output. The commenter asked whether the objective is to obtain a single estimate for each needed parameter; whether each value is intended to be a "best estimate"; and whether there is any accounting for uncertainty in the parameter values?

Response: The physical and chemical properties are identified in Appendix B as listed in bullet point #1 of Section 2.7.1 in the draft scope. EPA plans to evaluate all sources cited in EPA's analysis plan according to the procedures and metrics described in OPPT's Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances (Docket No. EPA-HQ-OPPT-2021-0414).

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0029) compared the two sets of physical and chemical properties for D4 presented by (1) Kozerski et al. (1937) and Xu and Kropscot (2014) and (2) Panagopoulos Abrahamsson et al. (2020). The commenter noted that previous studies by Krogseth et al. and Panagopoulos Abrahamsson et al. have shown that when modeling the environmental fate of volatile methylsiloxanes in aquatic environments, the physical and chemical properties of Panagopoulos Abrahamsson et al. predict more accurately experimentally measured concentrations of D4 in sediments, while concentration predictions using the properties Kozerski et al. and Xu and Kropscott underestimate concentrations in sediments by more than 2 log units. The commenter asserted that (1) the calculations of persistence in aquatic environments Panagopoulos Abrahamsson et al. provide are closer to real world values and should be considered in calculations of persistence by EPA when assessing the environmental risk posed by D4, and (2) that the default should be to use the study that would best protect the environment.

Response: EPA will consider this approach for the D4 risk evaluation. The sources identified by the commenter are undergoing systematic review and will be evaluated according to the procedures and metrics described in EPA's Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances (Docket No. EPA-HQ-OPPT-2021-0414). Following the data evaluation, synthesis, and integration phases of systematic review, EPA will determine how specific physical and chemical property information will be used in the risk evaluation for D4.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0030) recommended EPA conduct uncertainty analysis when relying on models to estimate physical and chemical and environmental fate and transport properties, as well as environmental, consumer, and general population exposures as stated in the draft analysis plan (Section 2.7). The commenter noted that the deficiencies identified with the models include EPI Suite's lack of transparency in modeling physical and chemical properties. More specifically the commenter stated that one log octanol-water partitioning coefficient program that is used in EPI Suite, KOWWIN™, uses property estimates are less accurate for compounds with molecular weights that are different from those used in training. The commenter requested clarity as to whether EPA will use the newer, more transparent OPERA model for its estimation of physical and chemical properties and recommended that EPA outline its criteria for model selection and the specific steps to characterize uncertainty around any modeled inputs or outputs in the final D4 scope.

Response: EPA agrees that substances must be within the domain of the model, which is why EPI Suite v4.11 contains an update for organosilicon substances as described in Section 1.6 of the EPI Suite helpfile. The update improved the accuracy of KOWWIN and seven other models for predicting the physical and chemical properties of organosilicon substances. Detailed descriptions of the EPI Suite

models are provided in the helpfiles, many journal articles, and in the Science Advisory Board review of EPI Suite. EPA does consider OPERA estimates along with other physical and chemical property estimation models.

Related Comments:

- One commenter (EPA-HQ-OPPT-2018-0443-0028) asserted that the emission scenario on page 21 of *Supplemental File: Data Extraction and Data Evaluation Tables for Physical and Chemical Property Studies for D4 Degradants* (Docket No. EPA-HQ-OPPT-2018-0443-0025) is not realistic. The commenter suggested that a more realistic emission scenario should be used based on the conceptual model shown in Figure 2-15 of the main document, noting that the Level III fugacity model should be run separately without relying on estimates based on BIOWIN and to allow for incorporation of the measured inputs of degradation half-lives and realistic emission rates.

- The same commenter (EPA-HQ-OPPT-2018-0443-0028) noted that since actual data exist that demonstrate D4 degrades, measured values should be used for the modeling for better estimation of mass distribution in the environment; measured values of half-lives in water, soil, and sediment are 93.6, 127.2, and 8,760 hours, respectively.

Response: These important corrections have been made and predicted fate endpoints have been removed from the Supplemental File: Data Extraction and Data Evaluation Tables for Physical and Chemical Property Studies for D4 Degradants document (Docket No. EPA-HQ-OPPT-2018-0443-0024).

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0028) stated that the reference to linear siloxanes in Appendix C of the draft scope document is in error and claimed that the correct reference is linear dimethylsiloxane-α,ω-diol oligomers (silanols). The commenter suggested that the table should clarify that "linear dimethylsiloxane-α,ω-diol oligomers are degradation products formed by the hydrolysis of D4 (or siloxanols) (Durham, 2005; EC/HC, 2008; Brooke, 2009)."

Response: EPA replaced linear siloxane with linear dimethylsiloxane-α,ω-diol oligomers (silanols). However, the reasonably available information supports the conclusion that dimethylsilanediol (DMSD) is the final hydrolysis product. For example, Durham (2005) states on page 20 "…D4 is readily transformed via hydrolysis to a smaller, more polar compound, likely $Me_2Si(OH)_2$." Brooke et al. (2009) state on page 53: "The final product from this process is dimethylsilanediol." Environment Canada and Health Canada (2008) on page 13 states: "….dimethylsilanediol (DMSD) was the final hydrolysis product." These findings may be updated as EPA evaluates and integrates additional information obtained through systematic review methods and provided during the public comment period for the draft risk evaluation.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0028) requested EPA clarify the source of information that D4 may be imported in a dry powder form. Based on the physical and chemical properties of D4, it is not possible for D4 to occur in a dry powder form.

Response: EPA has received a submission from a company claiming that their name is confidential business information (CBI) under the Chemical Data Reporting (CDR) Rule, under TSCA, indicating that D4 is imported as a dry powder.

1.5 Exposure

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0030) stated that it is unclear if EPA has abandoned their previous practice of excluding pathways governed by other statutes and urged the Agency to explicitly state its 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. The commenter pointed to the example of Table_Apx A-7 in Appendix A, which indicates that EPA intends to treat environmental pathways addressed by other EPA-administered statutes as "supplemental pathways," which EPA refers to as pathways addressed by other EPA administered statutes.

Response: The Conceptual Model for Environmental Releases and Wastes: Environmental and General Population Exposures and Hazards, includes all exposure pathways in the scope of the risk evaluation. EPA does not plan to exclude exposure pathways due to overlap with other EPA-administered statues or regulatory programs or other EPA-administered laws. Pathways regulated by other EPA administered statues are no longer considered only as "supplemental pathways." Table Apx_A-7 and language referring to "supplemental pathways" has been removed from the final scope document.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0028) suggested EPA clarify the information sources that support the inclusion of the receptors and pathways identified in the Executive Summary, including the specific information source that demonstrates that D4 can deposit on surfaces such as a dust particle, as not all receptors/pathways are appropriate given the physical and chemical properties of D4. The commenter stated that it is critical to conduct a thorough evaluation of any reported D4 concentrations to ensure the appropriateness of the collection, handling, and analytical procedures associated with any reported presence of D4.

Response: EPA will include a description of information sources used in the determination of pathways of exposure and receptors when building exposure scenarios during development of the risk evaluation as well as after completing the data evaluation, extraction, and integration phases of the systematic review process as described in EPA's Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances (Docket No. EPA-HQ-OPPT-2021-0414).

1.5.1 Consumer Exposure

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0029) claimed the consumer exposure section of the draft analysis plan (Section 2.7.2.4) does not include identification of the characteristics of the consumers of D4-containing products, which is necessary information to identify PESS. The commenter stated that although the section mentions review of reasonably available population- or subpopulation-specific exposure factors and activity patterns to determine if PESS need to be further refined, it is not clear whether this task includes determination of who the consumers are. The commenter inquired (1) whether consumer products containing D4 are used by children; (2) what are the demographic characteristics (*e.g.*, race/ethnicity, income) of the consumers of D4 products; and (3) whether exposure levels are likely to be correlated with any demographic variables? The commenter stated that these are important questions that should be considered in the analysis plan.

Response: The commenter's suggestions will be considered during the risk evaluation of D4. Consumer exposure considerations are described in Sections 2.3.6 and 2.6.2, Figure 2-14, and Appendix G. Section 2.7.2.4 in the analysis plan does not contain a detailed description of the scenarios, which will be developed for the draft D4 risk evaluation following the data evaluation, synthesis, and integration phases of systematic review. PESS considerations are also described in Section 2.5 of the scope document and in Section 1.2 of this Response to Public Comments document.

Related Comments:

- One commenter (EPA-HQ-OPPT-2018-0443-0028) noted that "toys, playground, and sporting equipment: Oral exposure through mouthing of toys" was included in the D4 request for MRRE, where data for infant bottle nipples/sipper tubes/straws were used as a surrogate for pacifiers/teethers and infant toys. The commenter asserted that use of mouthguards as well as chin and goggle straps in sporting equipment will not result in additional oral exposures beyond what is already assessed in the draft risk evaluation included with the D4 MRRE request.

- The same commenter (EPA-HQ-OPPT-2018-0443-0028) pointed out that in the draft risk evaluation included with the D4 MRRE request, dermal exposure to D4 was not considered relevant in the condition of use for animal grooming products in both commercial and consumer uses, due to the lack of dermal toxicity and very low dermal absorption. The commenter stated that dermal exposure to D4 from this use will be much less than the exposure representing the greatest exposure to D4 through consumer use (*e.g.*, body lotion for adults) that was addressed in the draft risk evaluation included with the D4 MRRE request.

Response: EPA plans to consider all relevant exposures. The Agency's systematic review process may identify additional data related to oral, mouthing, and dermal exposure from use of toys, playground, sporting equipment, and animal grooming products. Additional information includes applicable chemical-specific oral or dermal exposure data, experimental studies, and exposure models. EPA plans to evaluate all reasonably available information, and if it determines that the exposure is negligible, such results will be explained in the draft risk evaluation.

1.5.2 Occupational Exposure and Environmental Releases

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0029) expressed concern that the draft analysis plan for occupational exposures (Section 2.7.2 of the draft scope document) provides very limited information. The commenter stated that the plan does not identify routes of exposure such as inhalation or dermal, exposure durations as acute or chronic, specific metrics or measures, nor an approach for representing exposure variability.

Response: Appendix F, which is referenced in this section of the analysis plan, contains an initial mapping of exposure scenarios that provides routes of potential exposure(s) the EPA plans to evaluate. As stated in Section 2.7.2.3 #6, "EPA plans to refine mapping or grouping of occupational exposure scenarios based on factors (e.g., process equipment and handling, magnitude of production volume used, and exposure/release sources) corresponding to conditions of use as additional information is identified." EPA will evaluate the weight of the scientific evidence and use professional judgement to determine the exposure durations to evaluate for a given activity, process, and/or condition of use as a whole. The extent of variability and uncertainty will be determined during the data evaluation, synthesis, and integration stages of systematic review.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0029) asserted that Section 2.7.2.3 #7 of the draft analysis plan is unclear regarding what will be assessed in the weight of evidence evaluation, and that it provides very little information regarding the expected outcome and products of the occupational exposure analysis. The commenter recommended to outline the expected outputs of the occupational exposure analysis that will be provided in the risk evaluation and to include a concise statement indicating the exposure pathways and routes, exposure durations, and exposure metrics to be assessed is needed—along with indications of how uncertainty and variability will be represented (*e.g.*, presentation of central estimates and/or upper bound estimates).

Response: The expected outcome of the risk evaluation, as stated in Section 1 of the draft scope document, is to "determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other non-risk 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." Appendix F is an initial mapping of exposure scenarios that provides an overview of the exposure pathways and routes that EPA plans to evaluate, and these exposure scenarios may be updated if warranted by the weight of the scientific evidence. The extent of variability and uncertainty will be determined during the data evaluation, synthesis, and integration stages of systematic review.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0030) disagreed with EPA's approach to occupational exposure scenario development through mapping or grouping of conditions of use to exposure scenarios. The commenter asserted that TSCA does not allow EPA to ignore data simply because they have not been tied to a particular condition of use and that data that cannot be attributed to specific conditions of use are still relevant to determining whether the chemical substance presents an unreasonable risk. The commenter provided the example of biomonitoring data that are not able to be associated with a condition of use or grouping of conditions of use.

Response: Reasonably available biomonitoring data will be considered for the risk evaluation and, where possible, EPA will characterize exposure as it relates to the TSCA conditions of use. During the data integration phase, EPA may find information that is not specific to a condition of use and may be used in any aggregate and background analysis.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0030) asserted that EPA's proposed approach for estimating inhalation exposure to ONUs will underestimate their exposure, as it assumes that they will always stay outside of the near-field zone of the chemical's use. The commenter recommended that to the extent possible, EPA should acquire information on the location of ONUs for specific conditions of use, and at a minimum, use a more conservative default assumption.

Response: Exposures for ONUs can vary substantially. In previous EPA OPPT risk evaluations, most data sources did not sufficiently describe the proximity of these employees to the exposure source. As such, exposure levels for the "occupational non-user" category may have high variability depending on the specific work activity performed. It is possible that some employees categorized as ONUs have exposures similar to those in the "worker" category depending on their specific work activity pattern. All reasonably available information regarding the locations and activities of ONUs will be considered during the risk evaluation.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0030) recommended that when assessing exposure with the use of personal protective equipment (PPE), EPA should take into account PPE's limited efficacy even when its use is required. The commenter also recommended that EPA should obtain the information needed to account for such real-world limitations of PPE by collecting or requiring the development of empirical data to assess the actual extent of PPE use and the resulting exposure reduction, starting with examining the eight PPE occupational exposure studies identified through the literature search in Figure 2-6.

Response: EPA does not plan to make risk determinations for D4 based on assumptions about the use of PPE or other control technologies. However, EPA plans to develop exposure scenarios with and without the use of PPE or other control technologies to inform any potential risk management required for workers or ONUs. OSHA recommends employers utilize the hierarchy of controls to address hazardous

exposures in the workplace. The hierarchy of controls strategy outlines, in descending order of priority, the use of elimination, substitution, engineering controls, administrative controls, and lastly PPE. EPA plans to identify the engineering controls and PPE relevant to occupational exposure scenarios based on reasonably available information on control technology and effectiveness. Furthermore, to better inform any potential risk management, EPA plans to assess in the risk evaluation worker exposure pre- and post-implementation of engineering controls (e.g., local exhaust ventilation) and with and without the use of PPE (e.g., respirators). All reasonably available information, including the studies already included in Figure 2-6, will be evaluated according to systematic review procedures and metrics described in EPA's Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances (Docket No. EPA-HQ-OPPT-2021-0414). For the purpose of the draft D4 risk evaluation, EPA will make assumptions about potential PPE use and efficacy based on the outcome of the systematic review of all reasonably available information for PPE.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0030) noted that direct ingestion by workers and ONUs is an exposure route that is not reflected in the Conceptual Model for Industrial and Commercial Activities and Uses (Figure 2-13), and that this route is also omitted in analysis plan for workers and ONUs. The commenter recommends that direct ingestion should be systematically considered, citing Ng et al. (2014), who found that, on average, workers had hand-to-mouth contact frequency at 6.3 events per hour and even higher hourly rates when between tasks. The authors also found that use of PPE such as gloves did not change the contact frequency and that this route of exposure was particularly important for workers who smoke or bite their nails.

Response: The referenced article will undergo EPA's systematic review process and will be considered for inclusion to the D4 risk evaluation. Currently, for certain conditions of use, EPA plans to consider inhalation exposure to dust/particulates for workers and ONUs. As inhalation exposure to dust/particulates might occur, EPA plans to consider potential exposure for particulates that deposit in the upper respiratory tract from inhalation exposure and could be ingested via the oral route. EPA acknowledges that although workers may inadvertently transfer chemicals from their hands to their mouths, the frequency and significance of this exposure route are dependent on several factors, including the workers' habits and personal hygiene, which are difficult to predict. At the time of this response, the systematic review process remains in progress. EPA will rely on the results of the systematic review process to inform the assessment and use that data as appropriate, in conjunction with professional judgement, to determine the types of exposures that could be reasonably expected to occur as a normal part of a process or activity.

1.6 Human Health Hazards

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0028) requested that EPA clarify the approach the Agency intends to follow to determine whether and how to apply "alternative approaches including consideration of susceptibility factors in the application of an intraspecies uncertainty/variability factor in the risk characterization."

Response: The cited sentence explains that one alternative approach for determining intraspecies uncertainty/variability factor (UFH) is inclusion of information on susceptibility factors. In making the UFH determination, the Agency will consider quantitative information on susceptibility. This consideration is dependent on data quality evaluation of the reasonably available information on susceptibility.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0029) recommended EPA make additional improvements to the text concerning dose-response analysis in Section 2.7.3.2 of the draft scope

document. Specifically, the commenter recommended (1) the deletion of the dose-response text (*i.e.*, paragraphs 2 and 3) from item 3 as dose-response is addressed more clearly in item 4; item 3 would then be focused on hazard identification, leaving dose-response assessment to item 4; some of the text deleted from item 3 could be restored under item 4 if appropriately revised; (2) in paragraph 2, the reference to margin of exposure (MOE) should be replaced with improved methods described above; (3) the last sentence of this paragraph, concerning "if additional information on the identified hazard endpoints are not reasonably available" is unclear regarding the intended approach and should be deleted entirely; and (4) in paragraph 3, the initial sentences regarding mode of action and human relevance are confusing without the broader context of carcinogen hazard assessment and should be replaced with text representing a broader perspective on evaluation of cancer hazard and selection of a cancer hazard descriptor; therefore, the commenter suggested moving this revised paragraph to item 4.

Response: The analysis plan in the draft scope outlines the general science approaches that EPA plans to use for human health hazard and risk characterization. The analysis plan is not detailed as it is based on EPA's knowledge of D4 to date, including the full-text screening results of reasonably available information identified through literature searches as well as the information included in the SEHSC submission. Accordingly, the analysis plan for the scope document reflects the plan for evaluation based on the level of systematic review completed to this point. EPA plans to develop the detailed methodology and specific analyses for the human health hazard assessment after completing the data evaluation, synthesis, and integration stages of systematic review, taking into account these suggested improvements.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0028) supported EPA's approach described in the draft scope for considering the persistence, bioaccumulation, and toxicity (PBT) potential of substances in the context of the D4 risk evaluation.

Response: EPA appreciates the comment supporting the risk evaluation approach to PBT potential and continues to implement the requirements of the Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act (Risk Evaluation Rule) (40 CFR Part 702).

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0029) claimed that the Human Health Hazards section of the analysis plan (Section 2.7.3.2) is very general and does not incorporate readily available information on toxicity endpoints for D4. The commenter noted that previous assessments of D4 by the European Chemicals Agency (ECHA) and Health Canada have identified reproductive endpoints, respiratory irritation, increased liver weight, decreased fetal body weight, and decreased fetal liver weight as hazards of D4. The commenter also recommended the analysis plan incorporate the information on health effects studies presented in Figure 2-10 (Literature Inventory Heat Map) of the draft scope document and that this section of the analysis plan needs to identify the objectives and the expected outputs of the "weight of the scientific evidence" evaluation.

Response: The purpose of Section 2.7.3.2 is not the identification of hazards for D4, but instead to provide a framework of the analysis plan to be used by EPA for evaluation of the reasonably available information for hazard identification. Figure 2-10 represents the references obtained from publicly available databases and from the SEHSC submission, which EPA plans to analyze using the population, exposure, comparator, and outcome (PECO) criteria defined in the draft scope Table_Apx A-4. The potential human health hazards identified by EPA using automated techniques during data screening are listed in Section 2.4.2 of the scope document.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0030) asserted that EPA must evaluate D4's potential cancer hazard if there is evidence of potential carcinogenicity. The commenter further asserted that EPA's current approach of relying on MOA to determine the relevancy of animal data to humans 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, the commenter recommended EPA use animal toxicological data to characterize D4 cancer risk to humans, and that if there is any evidence of carcinogenicity in animal data, then those data are entirely relevant to characterizing potential cancer risk to humans.

Response: The analysis plan explains that EPA will use MOA analyses to (1) identify cancer MOA for all cancer endpoints, and (2) determine the human relevance of the animal cancer data for all cancer endpoints. EPA plans to determine the appropriate approach for quantitative cancer assessment in accordance with the U.S. EPA Guidelines for Carcinogen Risk Assessment (U.S. EPA, 2005).

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0030) suggested EPA employ a unified framework for dose-response assessment of cancer and non-cancer endpoints, as was recommended by the National Academies' report, *Science and Decisions: Advancing Risk Assessment* (NRC, 2009). The commenter stated that a unified approach for dose-response modeling could include 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. The commenter concluded that a description of such a unified approach to dose-response assessment of cancer and non-cancer endpoints should be included in the final D4 scope.

Response: The suggestion for employing a unified framework for dose-response assessment of cancer and non-cancer endpoints is a valid point for Agency consideration. TSCA sections 26(h) and (i) require EPA, when conducting risk evaluations, to use scientific information, technical procedures, measures, methods, protocols, methodologies, and models consistent with the best available science and to base its decisions on the weight of the scientific evidence. The dose-response assessment of cancer and non-cancer endpoints will be conducted in accordance with EPA's risk assessment guidelines and peer review. The purpose of peer review is for the independent review of the science underlying the risk assessment, including assessment of dose-response and risk characterization.

1.7 Environmental Hazards

Related Comments:

- One commenter (EPA-HQ-OPPT-2018-0443-0028) stated DMSD would be classified as "practically non-toxic" based on the acute toxicity data for aquatic organisms according to the EPA classification scheme used in the pesticides program.

- The same commenter (EPA-HQ-OPPT-2018-0443-0028) reported that DMSD is a known mammalian metabolite of D4 and has been detected as a metabolite via intravenous, oral, and inhalation administration of D4. The commenter stated that data indicate that DMSD is systemically available following exposure to D4 in the toxicological studies of D4 and is also the major metabolite of D4. The commenter concluded that as such, (1) any toxicity studies on D4 would account for any toxicity associated with DMSD following a direct exposure to D4, and (2) any additional exposure from DMSD formed in the environment following release of D4 to the environment would be minor in comparison to the direct exposure to D4 in standard high dose toxicological studies.

Response: As reported in Section 2.3.2 of the scope document, EPA has identified the presence of DMSD in the environment. All reasonably available toxicity information received for DMSD will be considered in the draft risk evaluation for D4 pending the data evaluation, synthesis, and integration procedures described in EPA's Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances (Docket No. EPA-HQ-OPPT-2021-0414).

1.8 Degradation Products

Related Comments:

- One commenter (EPA-HQ-OPPT-2018-0443-0028) requested that EPA include additional information in the scope about how the Agency plans to evaluate the potential degradation products in the D4 risk evaluation. The commenter also recommended the Agency include such additional information on pages 35, 36, 38, and 39 of the draft scope, including how data on DMSD and other degradation products will be assessed and used to inform the risk evaluation for D4.

- Another commenter (EPA-HQ-OPPT-2018-0443-0029) urged EPA to assess risk from human and environmental exposure to D4 degradation products such as DMSD, and that the scope document must be revised accordingly. The commenter noted that not fully accounting for cumulative risk assessment with metabolites and potential mixtures will underestimate the health risks of D4. The commenter recommended that the analysis plan describe how information on the D4 degradation products submitted during the public comment period will be used in the risk evaluation, asserting that risks from exposure to DMSD and other breakdown products must be accounted for in assessing the risks of D4.

Response: In the draft scope, EPA identified studies reporting that D4 degrades into DMSD in water, soil, and sediment via different intermediate degradants under specific field and laboratory conditions. Concentrations of DMSD in water, soil, and sediment could provide relevant information for environmental exposure to D4 degradants. Therefore, EPA requested information from the public on the environmental concentration of DMSD and the intermediate degradation products of D4 in water, soil, and sediment. Information on DMSD was provided during the public comment period and will be considered in the risk evaluation for D4. This information will be evaluated according to the procedures and metrics described in EPA's Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances (Docket No. EPA-HQ-OPPT-2021-0414) Data and information that meet EPA's evaluation criteria will be included in the risk evaluation for D4 as described in the analysis plan (Section 2.7) of the final scope.

Related Comments:

- One commenter (EPA-HQ-OPPT-2018-0443-0028) recommended on pages 14 and 24 of the draft scope that EPA identify the degradation products octamethyltetrasiloxanediol (CASRN 3081-07-0), hexamethyltrisiloxanediol (CASRN 3663- 50-1), tetramethyldisiloxanediol (CASRN 1118-15-6) and DMSD (CASRN 1066- 42-8) as intermediate degradation products, not final degradation products.

- The same commenter (EPA-HQ-OPPT-2018-0443-0028) suggested that the title of the supplementary document, *Supplemental File: Data Extraction and Data Evaluation Tables for Physical and Chemical Property Studies for D4 Degradants* (Docket No. EPA-HQ-OPPT-2018-0443-0025) should be revised to "intermediate degradation products" and not "final degradation products" of D4.

Response: EPA uses the term "degradation products" to differentiate these substances from D4 and does not characterize whether the degradation products are intermediate or final products.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0028) urged EPA to consider the rates of formation and disappearance of the four intermediates identified in the draft scope to assess the relevance of environmental exposure and fate and ultimate inclusion into the D4 risk evaluation. The commenter noted that this is a step-wise process where these listed substances are intermediates in the degradation pathway of D4, and as intermediates, it is important to look at the rates of formation and disappearance to assess the importance of environmental exposure. Finally, the commenter suggested that DMSD be referred to as an intermediate instead of "end-product" since it will ultimately degrade.

Response: The reaction sequence of D4 undergoing step-wise degradation through octamethyltetrasiloxanediol (CASRN 3081-07-0), hexamethyltrisiloxanediol (CASRN 3663-50-1), tetramethyldisiloxanediol (CASRN 1118-15-6), and into the stable end-product DMSD (CASRN 1066-42-8) is described in Section 2.3.2 on Page 35 of the final scope document. In Section 2.3.4 on page 36 and Section 2.3.7 on page 38, it states that D4 degrades into DMSD in water, soil, and sediment via different intermediate degradants under specific field and laboratory conditions. In Section 2.4.1 and 2.4.2 on page 39 it states that D4 degrades into DMSD in water, soil, and sediment via different intermediate degradants under various conditions. These statements were made to justify the request for information on DMSD and the intermediates. The only information received during the public comment period was for DMSD, including information stating that "the biodegradation of DMSD is an unsettled issue with some evidence that DMSD may undergo biodegradation to form methylsilanetriol and CO_2 under some conditions in the environment while other studies looking at more standard biodegradation have reported that no significant DMSD biodegradation could be observed" (EPA-HQ-OPPT-2018-0443-0028). This information will undergo data screening and evaluation during systematic review and will be considered for inclusion in the risk evaluation as described in the analysis plan (Section 2.7) of the final scope.

1.9 Risk Characterization and Risk Determination Approaches

Related Comments:

- One commenter (EPA-HQ-OPPT-2018-0443-0029) recommended that the approaches to dose-response assessment and risk characterization in the analysis plan be clarified and expanded.

- The same commenter (EPA-HQ-OPPT-2018-0443-0029) asserted that Section 2.7.4 of the analysis plan lacks any indication of how integration of exposure estimates from measured and/or modeled data with hazard data to characterize risk to human health will be done, which the commenter contended is a critical omission. The commenter stated that based on past practice, it appears that risk characterization will consist of computing an MOE and comparing this value to a benchmark MOE. The commenter recommended combining any exposure estimates with the outputs of probabilistic dose response methods to estimate non-cancer population risks expressed as frequency of cases in the exposed population (*e.g.,* "X cases per 1,000 exposed").

Response: The dose-response and risk characterization approaches to be employed are dependent on the EPA evaluation of the reasonably available information using the PECO criteria presented in Appendix A. EPA plans to evaluate hazard data to determine the type of dose-response modeling that is appropriate, in accordance with EPA guidance (U.S. EPA, 2012) (U.S. EPA, 2011) (U.S. EPA, 1994).

Related Comments:

- One commenter (EPA-HQ-OPPT-2018-0443-0029) recommended that EPA explain how the Agency will integrate exposure estimates with hazard data for risk characterization in the risk characterization section (Section 2.7.4) of the scope document. The commenter noted that the absence of any text regarding the approach leads to uncertainty and increased potential for adverse comments when the draft risk evaluation is subject to peer review and public comment. At a minimum, the analysis plan should disclose any approaches that EPA is considering for risk characterization.

- The same commenter (EPA-HQ-OPPT-2018-0443-0029) pointed out that no indication is given in the draft analysis plan of how upper- or lower-bound estimates of risk will be determined when presenting expected risk or central estimate of risk for the PESS affected. The commenter contended that the analysis plan needs to describe the nature of the uncertainty or variability to be addressed and should identify the parameters to be assessed with varying values to derive upper- and lower-bound estimates of risk.

Response: The analysis plan in the draft scope provides a summary of the approaches that EPA plans to use for risk characterization. The analysis plan for the final scope document reflects the plan for evaluation based on the level of systematic review completed to this point. The clarity and completeness of the analysis plan for risk characterization are influenced by the upcoming data evaluation, synthesis, and integration stages of systematic review. Regardless of the level of complexity or information, the risk characterization will be prepared in a manner that is transparent, clear, consistent, and reasonable (TCCR) (U.S. EPA, 2000) and consistent with the requirements of the Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act (82 FR 33726, July 20, 2017).

Related Comments:

- One commenter (EPA-HQ-OPPT-2018-0443-0029) asserted that continued use of the MOE approach in the D4 risk evaluation would not fully satisfy the requirements of TSCA to use the best available science and to assess risks to PESS, and that it will not provide the most useful information for risk management decision-making in the case of an unreasonable risk determination. To meet these needs, the scope document should commit to incorporating probabilistic methods for dose-response analysis and using the outputs of the probabilistic methods for risk characterization. These methods will substantially improve TSCA risk evaluations by enabling EPA to quantify how population risk varies at differing levels of exposure.

- The same commenter (EPA-HQ-OPPT-2018-0443-0029) stated that methods to quantify risks of non-cancer effects have been described by authoritative bodies such as the National Academies of Science and World Health Organization and demonstrated in published case studies and that such methods, which provide estimates of the number of cases of disease in a population with a given level of exposure, are necessary for (1) a complete characterization of non-cancer risk; (2) for a complete characterization of any health inequities that may be associated with exposure to D4; and (3) to support economic analysis of the benefits of any risk management actions that would follow an unreasonable risk determination.

Response: The suggestion for employing probabilistic methods for dose-response analysis of cancer and non-cancer endpoints is a valid point for Agency consideration during dose-response analysis, after the ongoing hazard data evaluation is completed. TSCA sections 26(h) and (i) require EPA, when conducting risk evaluations, to use scientific information, technical procedures, measures, methods,

protocols, methodologies, and models consistent with the best available science and to base its decisions on the weight of the scientific evidence. EPA plans to evaluate hazard data to identify information on factors that influence susceptibility and to conduct dose-response analysis for non-cancer and cancer endpoints in accordance with agency guidelines. Peer review will be conducted on the draft risk evaluation. The purpose of peer review is for the independent review of the science underlying the risk assessment, including assessment of dose-response and risk characterization.

Peer review will be conducted in accordance with EPA's regulatory procedures for chemical risk evaluations, including using EPA's Peer Review Handbook and other methods consistent with section 26 of TSCA (see 40 CFR 702.45).

1.10 Data Gathering and Information Considered

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0030) urged EPA to add D4 to Toxics Release Inventory (TRI) to reduce uncertainty that results from its reliance on modeled or surrogate data. If immediately initiating the addition of D4 to TRI will not yield information before EPA completes the D4 risk evaluation, then the commenter asserts the TRI-provided environmental release data will still be very useful for other reasons.

Response: Amending the TRI database is beyond the scope of the risk evaluation for D4. The TRI program was authorized by section 313 of the 1986 Emergency Planning and Community Right-to-Know Act (EPCRA). Any additions or removals of chemicals in the TRI would occur pursuant to EPCRA section 313 and its associated regulatory authority. As the commentor notes, the notice-and-comment process necessary to add D4 to TRI would not result in additional relevant information being made available to EPA within the timeframe of this action. EPA intends to complete the D4 risk evaluation before any data from TRI reports could reasonably be made available to the Agency.

Related Comments:

- One commenter (EPA-HQ-OPPT-2018-0443-0028) noted that consistent with 40 CFR 702.37(e)(6)(ii)(B), in granting the D4 MRRE request, EPA was required to determine that it had all the information needed to conduct the risk evaluation on the conditions of use that were the subject of the request; and the October 6, 2020, letter from EPA granting the D4 MRRE request states "EPA has also concluded that the Agency has the information needed to conduct a risk evaluation on D4."

- Another commenter (EPA-HQ-OPPT-2018-0443-0030) stated that EPA must not rely solely on voluntary information—especially from the general public—to fill data gaps and that EPA needs to use its TSCA authorities as soon as possible.

- The same commenter (EPA-HQ-OPPT-2018-0443-0030) stated that EPA needs to (1) identify significant information gaps on hazards or exposures; (2) promptly use its authority under TSCA section 4(a)(2) to require testing; (3) promulgate reasonable regulations under section 8 to obtain information about hazards, exposures, conditions of use, and more; (4) require manufacturers and processors to report a list of health and safety studies for a chemical substance or mixture under section 8(d); and (5) subpoena the production of reports, documents, and other chemical information as necessary.

- The same commenter (EPA-HQ-OPPT-2018-0443-0030) recommended that EPA use information authorities to fill identified data gaps regarding population-specific exposure factors; take advantage of publicly available sources such as NHANES (National Health and Nutrition

Examination Survey) to ascertain where there may be differential exposures across different demographic characteristics and internal resources such as the CompTox chemicals dashboard; and obtain information directly from PESS groups as soon as possible (*e.g.*, fenceline communities, environmental justice groups, tribal communities).

Response: Under 40 CFR 702.37(b)(4), the MRRE must include, "a list of all the existing information that is relevant to whether the chemical substance, under the circumstances identified by the manufacturer(s), presents an unreasonable risk of injury to health or the environment. The list must be accompanied by an explanation as to why such information is adequate to permit EPA to complete a risk evaluation addressing the circumstances identified by the manufacturer(s)." Under 40 CFR 702.37(e), EPA may identify additional conditions of use to be included in the risk evaluation, including those identified in public comments. In reviewing MRRE submissions, EPA determines whether the data in the submission is sufficient to conduct the risk evaluation on the conditions of use that were subject to the request. For data needs identified during the risk evaluation, EPA may use the Agency's TSCA authorities under sections 4, 8, or 11, as appropriate. For conditions of use where no measured data on releases are reasonably available, and when it may not be appropriate to use TSCA sections 4, 8, or 11 to collect such information (see, e.g., the definition of "reasonably available information" in 40 CFR 702.33), EPA may use a variety of methods including release estimation approaches and assumptions in the Chemical Screening Tool for Exposures and Environmental Releases (ChemSTEER) (U.S. EPA, 2015a).

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0030) recommended EPA take advantage of other EPA programs to fill gaps identified in literature inventory heatmaps (Figures 2-6, 2-8, and 2-10) and the PICS tool (*e.g.*, mammalian *in vivo* hazard data, subchronic and chronic information, ecological *in vivo* acute plant studies).

Response: EPA aims to efficiently use Agency resources in completing its TSCA risk evaluations and avoid duplicating efforts taken pursuant to other Agency programs.

1.11 Systematic Review

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0030) urged EPA to release its draft systematic review protocol *a priori*, stating that Appendix A on the literature search methods is inadequate. The commenter also asserted that EPA must at least release its draft systematic review protocol before D4's scope is finalized. Any changes made to the draft protocol from the time it was applied to D4's draft scope must be documented.

Response: EPA has published the Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances (Docket No. EPA-HQ-OPPT-2021-0414).

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0028) noted that the draft risk evaluation included with manufacturer's request for the D4 risk evaluation (EPA-HQ-OPPT-2018-0443-0004) was prepared in accordance with EPA's Risk Evaluation Guidance, which the Agency was required to prepare per TSCA section 26(l)(5) and based on EPA's "Application of Systematic Review in TSCA Risk Evaluations," EPA Document #740-P1-8001 (May 2018) (U.S. EPA, 2018). In preparing its request for a D4 MRRE and deciding to move forward with the MRRE following EPA's grant decision, the commenter asserted that the Agency relied upon established EPA guidance and rules for preparing and conducting such risk evaluations. The commenter urged EPA to explain clearly why existing systematic review protocol/guidance would be inappropriate for D4 and what opportunity there will be for review/commenting on the approach prior to its implementation in the D4 MRRE. The commenter

also expressed concern over not being able to publicly comment on any departure or modification of the systematic review protocol as applied to D4 since the public comment period for the draft scope will have expired prior to EPA's release of the new draft systematic review protocol.

Response: In February 2020, the National Academies of Sciences, Engineering, and Medicine (NASEM) began their review of the Application of Systematic Review in TSCA Risk Evaluations (U.S. EPA, 2018) and associated materials. The Science Advisory Committee on Chemicals (SACC) and the public also provided comments on this this document and associated materials during the scientific peer review and during the public comment period for the first 10 risk evaluations. Major updates have been made to EPA's systematic review procedures in response the NASEM, SAAC, and public recommendations and comments as well as improvements identified by EPA. These revisions are contained in EPA's Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances, which was published for public comment on December 20, 2021 (Docket No. EPA-HQ-OPPT-2021-0414). This document contains additional information on the data evaluation, data extraction, and data integration phases of systematic review, which follow the scoping phase of the risk evaluation. SEHSC and all other stakeholders will have an opportunity to comment on these draft methods prior to the publication of the draft risk evaluation for D4. In addition, EPA provided the searching and screening methods used for D4 in Appendix A of the draft scope document, which was published for public comment on September 8, 2021 (Docket No. EPA-HQ-OPPT-2018-0443-0021). The results of those methods were and are presented in Section 2.1.2 of both the draft and final scope documents. In addition, stakeholders will have an opportunity to comment on the specific methods and approaches used in the D4 risk evaluation when EPA publishes the draft D4 risk evaluation for public comment.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0028) requested clarification for whether and how the Agency intends to use the results of four studies conducted by Industrial Bio-Test Laboratories, Inc. (IBT)—see Indus Bio Test Labs Inc. (1977; 1976; 1976, 1966)—given the widely reported issues involving data irregularities and fraud impacting studies conducted by that lab in the 1970s. The commenter claimed that these studies should be given little weight due to the scientific integrity issues that reportedly occurred at IBT.

Response: The IBT studies are part of the reasonably available information that will undergo systematic review based on PECO criteria defined in Appendix A. Based on information from EPA's 1983 Summary of the IBT Review Program, studies conducted by IBT had at least one invalid test. The EPA review also found that about two-thirds of the 1,200 individual IBT tests cannot be considered reliable. EPA will conduct a similar data quality evaluation process for all reasonably available information about D4 according to the procedures and metrics describe in EPA's Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances (Docket No. EPA-HQ-OPPT-2021-0414) to determine whether data are of sufficient quality for inclusion in the D4 risk evaluation.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0028) requested that EPA clarify the approach the Agency intends to follow to determine whether and how to use "data from alternative test methods (*e.g.*, computational toxicology and bioinformatics; high-throughput screening methods; data on categories and read-across; *in vitro* studies)," including the Agency's "strategy for using information, accepted science policies, models and screening methodologies." The commenter recommended these data be limited to results published in peer-reviewed papers and sources, and that EPA should ensure that any alternative test method has been properly validated to ensure that D4 and silicone chemistry are within the domain of the alternative test method. Additionally, the commenter requested that stakeholders have the opportunity review and comment on these approaches prior to such approaches being used for the risk evaluation on D4.

Response: All reasonably available information will be evaluated according to the procedures and metrics described in EPA's Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances (Docket No. EPA-HQ-OPPT-2021-0414), which was published for public comment on December 20, 2021. In addition, stakeholders will have an opportunity to comment on the specific methods and approaches used in the D4 risk evaluation when EPA publishes the draft D4 risk evaluation for public comment.

2 RISK MANAGEMENT

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0026) expressed concerns over how the D4 risk evaluation and any future associated risk management actions would affect the silicone rubber seal industry, stating that this would have a devastating impact on the medical, automotive, and aerospace industries, which uses these types of seals.

Response: As part of the risk evaluation, EPA will determine whether or not the chemical substance presents an unreasonable risk of injury to health or the environment, including an unreasonable risk to a PESS identified as relevant to the evaluation, under the conditions of use. As part of this process, EPA must exclude consideration of costs or other non-risk factors (40 CFR 702.43(a)(3)). If the chemical is determined to present unreasonable risk, then the Agency will initiate proposed rulemaking under section 6(a) to require action to address such risk. As part of that rulemaking, an economic analysis would be conducted and EPA would be required to take into consideration the effects of the proposed regulatory action on the economy, among other requirements outlined in TSCA section 6(c), in selecting among regulatory approaches to address the unreasonable risk.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0028) requested that EPA clarify/confirm whether the approaches described in the draft scope are intended to be suitable for the development of a risk characterization and supporting analyses that can be used for the determination of whether D4 presents an unreasonable risk of injury to human health or the environment under each condition of use within the scope of the risk evaluation. The commenter stated that EPA's plans "to make the determination of unreasonable risk just once for the whole chemical when it is clear the majority of the conditions of use warrant one determination" appears to be at odds with the Risk Evaluation Rule (82 FR 33726 (July 20, 2017)). The commenter further requested that the Agency clarify whether EPA intends to abide by its prior statements and existing rules regarding the conduct of this risk evaluation. Specifically, will the Agency provide a risk determination for each condition of use within the scope of the risk evaluation? The commenter stated that changing a substantive requirement of the Risk Evaluation Rule "after-the-fact" and outside the notice/comment rulemaking process would deprive stakeholders of fair notice.

Response: In accordance with Executive Order 13990 ("Protecting Public Health and the Environment and Restoring Science to Tackle the Climate Crisis") and other Administration priorities, EPA must ensure that risk evaluations meet the requirements of TSCA, including conducting decision-making in a manner that is consistent with the best available science. As explained in more detail in the Cyclic *Aliphatic Bromide Cluster (HBCD); Draft Revision to the TSCA Risk Determination; Notice of Availability and Request for Comment (December 29, 2021)(Docket No. EPA-HQ-OPPT-2019-0237), EPA is providing notice and soliciting public input on a draft revision to the risk determination for HBCD that would make the unreasonable risk determination for HBCD as a whole chemical substance and would supersede the previous condition of use-specific no unreasonable risk determinations. In that document, EPA notes that either approach is permissible. EPA further notes that this action would pertain only to HBCD and, to the extent the Agency deems appropriate, additional similar actions that*

may follow would be specific to each of the chemical substances for which EPA has issued complete risk evaluations under TSCA section 6. EPA did not conduct new scientific analysis, and the risk evaluation continues to characterize risks associated with individual conditions of use in the HBCD risk evaluation. The Agency is simply changing the way in which it presents the overall unreasonable risk determination for HBCD as a whole chemical substance. Further, EPA has acknowledged a lack of specificity in the statute and inconsistency in the regulations with respect to the presentation of risk determinations in TSCA risk evaluations.

In the key regulatory provision from 40 CFR 702.47, the text explains that "[a]s part of the risk evaluation, EPA will determine whether the chemical substance presents an unreasonable risk of injury to health or the environment under each condition of uses [sic] within the scope of the risk evaluation, either in a single decision document or in multiple decision documents." For the unreasonable risk determinations in the first 10 risk evaluations, EPA applied this provision by making individual risk determinations for each condition of use evaluated as part of each risk evaluation document (i.e., the condition-of-use-specific approach to risk determinations). That approach was based on one particular passage in the preamble to the final Risk Evaluation Rule (see 82 FR 33726, 33744 (July 20, 2017)). However, in contrast to this portion of the preamble of the final Risk Evaluation Rule, the regulatory text itself and other statements in the preamble reference a risk determination for the chemical substance under its conditions of use, rather than separate risk determinations for each of the conditions of use of a chemical substance. For example, 40 CFR 702.31(a) states that the purpose of the rule is to establish "the EPA process for conducting a risk evaluation to determine whether a chemical substance presents an unreasonable risk of injury to health or the environment as required under TSCA section 6(b)(4)(B)." Likewise, there are recurring references to whether the chemical substance presents an unreasonable risk in 40 CFR 702.41(a). See, for example, 40 CFR 702.41(a)(6), which states: "[t]he extent to which EPA will refine its evaluations for one or more condition of use in any risk evaluation will vary as necessary to determine whether a chemical substance presents an unreasonable risk of injury to health or the environment." Notwithstanding the one statement about condition-of-use-specific risk determinations, the preamble to the final rule also contains support for a risk determination on the chemical substance as a whole. In discussing the identification of the conditions of use of a chemical substance, the preamble notes that this task inevitably involves the exercise of discretion on EPA's part, and, as "EPA interprets the statute, the Agency is to exercise that discretion consistent with the objective of conducting a technically sound, manageable evaluation to determine whether a chemical substance—not just individual uses or activities—presents an unreasonable risk" (82 FR 33726, 33729 (July 20, 2017)). Therefore, notwithstanding EPA's choice to issue condition-of-use-specific risk determinations to date, EPA interprets its risk evaluation regulation to also allow the Agency to issue whole-chemical risk determinations. Either approach is permissible under the regulation. EPA plans to consider the appropriate approach for each chemical substance risk evaluation on a case-by-case basis, taking into account considerations relevant to the specific chemical substance in light of the Agency's obligations under TSCA. The Agency expects that this case-by-case approach will provide greater flexibility in the Agency's ability to evaluate and manage unreasonable risk from individual chemical substances.

3 CONDITIONS OF USE

3.1 Classification of Conditions of Use

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0028) asserted that the additional uses identified by EPA in the draft scope that were not included in the D4 risk evaluation conducted and submitted by SEHSC with their request, while more specific in some cases, can be considered included in those uses identified in the more general categories presented in the draft risk evaluation included in SEHSC's request for the D4 MRRE (EPA-HQ-OPPT-2018-0443-0004).

Response: EPA is required to conduct MRREs in the same manner and using the same criteria as EPA uses in all TSCA risk evaluations, as outlined in the Risk Evaluation Rule (82 FR 33726 (July 20, 2017)). Some conditions of use for D4 were identified in the manufacturer request as circumstances on which EPA was requested to conduct a risk evaluation. EPA identified other conditions of use from information reported to EPA through its Chemical Data Reporting (CDR) Rule, published literature, and consultation with stakeholders for both uses currently in production and uses whose production may have ceased. EPA's methods for confirming conditions of use included searches in databases; review of SDS; and outreach with industry, states, and trade associations. EPA presented the proposed additions of these EPA-identified conditions of use and the basis for these proposed additions, along with the manufacturer request, for a 45-day comment period beginning in June 2020.

Related Comments:

- One commenter (EPA-HQ-OPPT-2018-0443-0030) asserted that EPA does not have discretion to "pick and choose" conditions of use, citing the Ninth Circuit ruling that EPA's regulations do not grant it discretion to exclude conditions of use from risk evaluations (*Safer Chemicals, Healthy Families v. U.S. Envtl. Prot. Agency, 943 F.3d 397, 425 (9th Cir. 2019)*). The commenter asserted that EPA wrongfully excluded spills and leaks as a condition of use, pointing to language in Figure 2-11, the Lifecycle Diagram. The commenter noted that exposures from leaks and spills in the workplace could be a substantial source of exposure, especially considering the potential for inhalation exposure from evaporation.

- The same commenter (EPA-HQ-OPPT-2018-0443-0030) recommended that the study inclusion criteria for D4 include all relevant information, such as exposures resulting from chemical spills or leaks, as well as from "background exposures" such as food packaging, personal care products, and medical applications, should be considered. The commenter asserted studies that measure exposures from background sources are relevant for the final scope and should be included.

Response: EPA does not consider spills, leaks, or accidental releases to constitute circumstances under which D4 is manufactured, processed, distributed, used, or disposed of, within TSCA's definition of "conditions of use." Congress specifically listed discrete, routine chemical life cycle stages within the statutory definition of "conditions of use," and EPA does not believe it is reasonable to interpret "circumstances" under which those substances are manufactured, processed, distributed, used, or disposed of to include uncommon and unconfined spills, leaks, or accidental releases for purposes of the statutory definition. Further, EPA does not generally consider spills, leaks, and accidental releases to constitute "disposal" for purposes of identifying a condition of use in the conduct of a risk evaluation. EPA therefore exercises its discretionary authority under TSCA section 3(4) to exclude spills, leaks, and accidental releases from the scope of the risk evaluation.

Exercising the discretion to not identify spills, leaks, and accidental releases of D4 as a condition of use is consistent with the discretion Congress provided in a variety of provisions to manage the challenges presented in implementing TSCA risk evaluation (see, e.g., TSCA sections 3(4), 3(12), 6(b)(4)(D), 6(b)(4)(F)). In particular, TSCA section 6(b)(4)(F)(iv) instructs EPA to factor into TSCA risk evaluations "the likely duration, intensity, frequency, and number of exposures under the conditions of use…," suggesting that activities for which duration, intensity, frequency, and number of exposures cannot be accurately predicted or calculated based on reasonably available information, including spills, leaks, and accidental releases, were not intended to be the focus of TSCA risk evaluations. And, as noted in the preamble to the Risk Evaluation Rule (82 FR 33726 (July 20, 2017)), EPA believes that Congress intended there to be some reasonable limitation on TSCA risk evaluations, expressly indicated by the direction in TSCA section 2(c) to "carry out [TSCA] in a reasonable and prudent manner."

Regarding "background exposures": TSCA's definition of "chemical substance" excludes "any food, food additive, drug, cosmetic, or device (as such terms are defined in section 201 of the Federal Food, Drug, and Cosmetic Act) when manufactured, processed, or distributed in commerce for use as a food, food additive, drug, cosmetic, or device." TSCA section 3(2). As stated in Section 2.2.2 of the scope document, although EPA would not regulate non-TSCA uses, consideration of 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 (e.g., as background exposures that would be accounted for, should EPA decide to evaluate aggregate exposures). EPA will determine during the risk evaluation whether to conduct background or aggregate analysis and what information would be needed for any background and aggregate analysis.

3.2 Additional Conditions of Use/Changes to Conditions of Use

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0027) suggested that EPA consider explicitly defining the use of D4 (CAS 556-67-2) as a potential impurity from the use of the substance in a manufacturing process aide (*e.g.*, antifoaming agent) in the risk evaluation document, since the substance would not be intentionally incorporated in the formulation, mixture, or reaction product. The commenter pointed out that the use of a processing aide can span multiple manufacturing categories with various applications, such as polymer manufacturing, paint and coating manufacturing, chemical product and preparation manufacturing, etc.

Response: Additional use information for this condition of use provided by the commenter was added to Section 2.2 and included as part of the use descriptions in Appendix E in the final scope document. EPA will address on a case-by-case basis circumstances where D4 is unintentionally present as an impurity in the final product.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0031) identified a large volume of potential uses in imported articles in the global automotive supply chain. The commenter plans to refine the data, collect additional information on non-dimensional uses, and then provide that to EPA in the near future.

Response: EPA will review additional data from the commenter when it is received.

3.3 Non-TSCA Uses

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0030) asserted that EPA must account fully for exposure through food consumption in all exposure settings as food is clearly consumed by people in both workplace and consumer exposure settings. The commenter stated that in occupational exposure settings, workers may transfer a chemical to food they then consume or may engage in some other hand-to-mouth activities that result in ingestion. They also noted that exposure through food is 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.

Response: EPA acknowledges that workers, consumers, and the general population may be exposed via ingestion of food. However, pursuant to TSCA section 3(2)(B)(vi), the definition of "chemical substance" does not include "any food, food additive, drug, cosmetic, or device (as such terms are defined in section 201 of the Federal Food, Drug, and Cosmetic Act) when manufactured, processed, or distributed in commerce for use as a food, food additive, drug, cosmetic, or device." EPA has determined that such uses of D4 do not constitute conditions of use and are not regulated under TSCA. Exposure scenarios will be developed based on the reasonably available information, weight of the scientific evidence, and fit-for-purpose approaches. Food consumption exposures may be included in background and aggregate exposure scenarios or incidental routes. Aggregate assessments may not be appropriate in all cases; for example, if there is not sufficient information that can be reliably modeled to perform additive ingestion exposures. EPA has not yet completed its data evaluation phase of systematic review of the reasonably available literature and is not yet able to discern the fit-for-purpose approach for D4.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0030) stated that EPA must consider all exposure pathways, even where those pathways may be regulated under other EPA authorities. The comment specifically noted 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."

Response: All activities related to preparing the chemical or products for distribution, such as loading, unloading, and repackaging, will be included in other conditions of use, or evaluated separately. EPA has removed the statements about assumptions pertaining to transportation in the Figure 2-11 caption. EPA plans to address transportation issues in the risk evaluation, as appropriate.

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0030) asserted that EPA must consider background exposure levels from non-TSCA conditions of use—specifically from food contact materials and additives, personal care products and cosmetics, and medical devices and drugs as background exposures. The commenter stated that EPA's exclusion of these activities from the scope of the risk evaluation would be inconsistent with scientific standards and weight of the scientific evidence requirements established in TSCA sections 26(h) and (i). The commenter urged EPA to unequivocally (1) state its plans to include such background exposures, (2) update the 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 in the final D4 scope.

Response: As stated in Section 2.2.2 of the scope document, although EPA would not regulate non-TSCA uses, consideration of the potential exposures from 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, should EPA decide to evaluate aggregate exposures). EPA will determine during the risk evaluation whether to conduct background or aggregate analyses and what information would be needed for any background and aggregate analysis, and the public will have an opportunity to review and comment on these specific approaches following publication of the draft risk evaluation.

4 SUBMITTED DATA AND INFORMATION

Comment: One commenter (EPA-HQ-OPPT-2018-0443-0028) provided a list of items they believe should be added to the Regulatory History in Appendix D of the D4 scope document.

Response: Submissions received under TSCA section 4 (including the International Trade Commission reports) and section 8 are accounted for in the Regulatory History for D4 included in Appendix D of the draft D4 Scope Document. EPA does not believe the following are regulatory actions and therefore did not include them in the Regulatory History: Memoranda of Understanding (MOUs), toxicity reports submitted to EPA Dockets, and the 2010 Chemical Action Plan. These sources will undergo the systematic review process and will be considered for inclusion in the risk evaluation following the data evaluation procedures and metrics described in EPA's Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances (Docket No. EPA-HQ-OPPT-2021-0414).

Comment: Three commenters (EPA-HQ-OPPT-2018-0443-0028; EPA-HQ-OPPT-2018-0443-0029; EPA-HQ-OPPT-2018-0443-0030) submitted a total of 96 information sources, including peer-reviewed literature, gray literature, industry studies or data, SDSs, and other reasonably available information.

Response: All of these sources will undergo deduplication with sources that are already undergoing EPA's systematic review process. All new sources will then follow the data and information screening, evaluation, extraction, synthesis, and integration processes as detailed in EPA's Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances (Docket No. EPA-HQ-OPPT-2021-0414).

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