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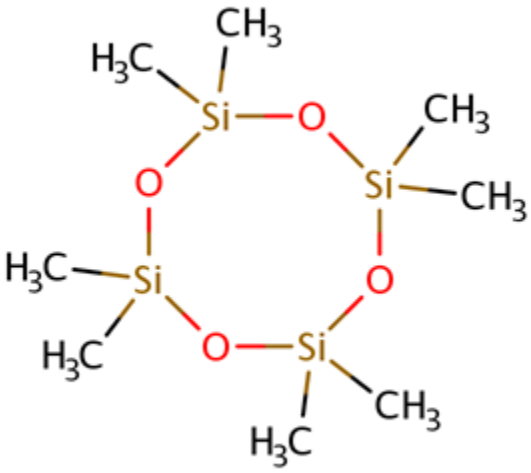
Office of Chemical Safety and
Pollution Prevention

United States
Environmental Protection Agency

Draft Scope of the Risk Evaluation for Octamethylcyclotetra- siloxane (Cyclotetrasiloxane, 2,2,4,4,6,6,8,8-octamethyl-)

(D4)

CASRN 556-67-2



August 2021

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Docket

Supporting information can be found in public docket, Docket ID: EPA-HQ-OPPT-2018-0443.

Disclaimer

Reference herein to any specific commercial products, process or service by trade name, trademark, manufacturer or otherwise does not constitute or imply its endorsement, recommendation, or favoring by the United States Government.

ABBREVIATIONS AND ACRONYMS

ACGIH	American Conference of Governmental Industrial Hygienists
ADME	Absorption, distribution, metabolism, and excretion
ADAF	Age-dependent adjustment factors
BAF	Bioaccumulation factor
BCF	Bioconcentration factor
BMF	Biomagnification factor
BOD	Biochemical oxygen demand
$BW^{3/4}$	Body weight scaling to the 3/4 power
CASRN	Chemical Abstracts Service Registry Number
CBI	Confidential business information
CDR	Chemical Data Reporting
CFR	Code of Federal Regulations
ChemSTEER	Chemical Screening Tool for Exposure and Environmental Releases
COC	Concentration(s) of concern
COU	Condition of Use
CPCat	Chemical and Product Categories
CPSC	Consumer Product Safety Commission
CSCL	Chemical Substances Control Law
CSF	Cancer slope factor
CWA	Clean Water Act
ECHA	European Chemicals Agency
EC	European Commission
EC_x	Effective Concentration that causes a response that is x% of the maximum
EPA	Environmental Protection Agency
ERG	Eastern Research Group
ESD	Emission Scenario Document
EU	European Union
FDA	Food and Drug Administration
FFDCA	Federal Food, Drug and Cosmetic Act
FR	Federal Register
GC	Gas chromatography
GDIT	General Dynamics Information Technology
GS	Generic Scenario
HAWC	Health Assessment Workplace Collaborative
HERO	Health and Environmental Research Online (Database)
Hg	Mercury
HHE	Health Hazard Evaluation
HQ	Headquarters
HSDB	Hazardous Substances Data Bank
ICF	ICF (a global consulting company)
IMAP	Inventory Multi-Tiered Assessment and Prioritisation (Australia)
IMIS	Integrated Management Information System
IUR	Inhalation Unit Risk
K_{OC}	Organic carbon: water partition coefficient
K_{OW}	Octanol: water partition coefficient
LC_{50}	Lethal Concentration of 50% test organisms
LOAEL	Lowest Observed Adverse Effect Level
LOEC	Lowest Observed Effect Concentration

MITI	Ministry of International Trade and Industry
MOA	Mode of action
MOE	Margin of exposure
MP	Melting point
MRSA	Maine Revised Statutes Annotated
NHANES	National Health and Nutrition Examination Survey
NICNAS	National Industrial Chemicals Notification and Assessment Scheme (Australia)
NIOSH	National Institute for Occupational Safety and Health
NITE	National Institute of Technology and Evaluation
NLM	National Library of Medicine
NOAEL	No Observed Adverse Effect Level
NOEC	No Observed Effect Concentration
NPDES	National Pollutant Discharge Elimination System
OCSPP	Office of Chemical Safety and Pollution Prevention
OECD	Organisation for Economic Co-operation and Development
OEL	Occupational Exposure Limit
ONU	Occupational non-user
OPPT	Office of Pollution Prevention and Toxics
OSF	Oral slope factor
OSHA	Occupational Safety and Health Administration
PBPK	Physiologically based pharmacokinetic
PBT	Persistent, bioaccumulative, toxic
PECO	Population, exposure, comparator, and outcome
PESO	Pathways and processes, exposure, setting or scenario, and outcomes
PESS	Potentially exposed or susceptible subpopulation
POD	Point of departure
POTW	Publicly owned treatment works
PPE	Personal protective equipment
PVC	Polyvinyl chloride
RCRA	Resource Conservation and Recovery Act
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals (European Union)
RESO	Receptors, Exposure, Setting or Scenario, and Outcomes
RQ	Risk quotient
SDS	Safety Data Sheet
SMILES	Simplified molecular-input line-entry system
SRC	SRC, Inc., formerly Syracuse Research Corporation
$T_{1/2}$	Half-life
TCCR	Transparent, clear, consistent, and reasonable
TIAB	Title and abstract
TMF	Trophic magnification factor(s)
TRI	Toxics Release Inventory
TSCA	Toxic Substances Control Act
U.S.C.	United States Code
VP	Vapor pressure
WS	Water solubility
WWTP	Wastewater treatment plant

EXECUTIVE SUMMARY

On March 19, 2020, EPA received a request, pursuant to 40 CFR 702.37, from Dow Silicones Corporation, Elkem Silicones USA Corporation, Evonik Corporation, Momentive Performance Materials, Shin-Etsu Silicones of America, Inc., and Wacker Chemical Corporation through the American Chemistry Council's Silicones Environmental, Health, and Safety Center (SEHSC), to conduct a risk evaluation for Octamethylcyclosiloxane (D4) (CASRN 556-67-2) (Docket ID: EPA-HQ-OPPT-2018-0443). This chemical substance is listed in the 2014 update to the Toxic Substances Control Act (TSCA) Work Plan as "octamethylcyclotetra- siloxane" and is assigned CA Index Name "Cyclotetrasiloxane, 2,2,4,4,6,6,8,8-octamethyl-." It is most commonly referred to as Octamethylcyclotetrasiloxane and will be abbreviated in this document as "D4." On June 17, 2020, EPA opened a 45-day public comment period to gather information relevant to the requested risk evaluation. EPA reviewed the request (along with additional information received during the public comment period) and assessed whether the circumstances identified in the request constitute conditions of use under 40 CFR 702.33 and whether those conditions of use warrant inclusion within the scope of a risk evaluation for D4. EPA determined that the request meets the applicable regulatory criteria and requirements, as prescribed under 40 CFR 702.37. The Agency granted the request on October 6, 2020.

The first step of the risk evaluation process is the development of the scope document, and this document fulfills the regulatory requirements under TSCA to issue a draft scope document as described in 40 CFR 702.41(c)(7). The draft scope document for D4 includes the following information: the conditions of use, potentially exposed or susceptible subpopulations (PESS), hazards, and exposures that EPA plans to consider in this risk evaluation, along with a description of the reasonably available information and science approaches EPA plans to use in the risk evaluation, a conceptual model, an analysis plan, and the plan for peer review of the draft risk evaluation for this chemical substance. EPA is providing a 45-day comment period on the draft scope document. Comments received on this draft scope document will help inform development of the final scope document and the risk evaluation.

General Information: D4 is a colorless, oily liquid with an annual total production volume in the United States in 2015 between 750 million and 1 billion pounds (U.S. EPA, 2020a).

Reasonably Available Information: To inform the development of this draft scope document, EPA leveraged the data and information sources identified within the SEHSC submission requesting EPA conduct the risk evaluation for D4 (Docket ID: EPA-HQ-OPPT-2018-0443), as well as any other data or information sources identified throughout the course of the submission and review process for this manufacturer requested risk evaluation. To further develop this draft scope document, EPA conducted a comprehensive search to identify and screen multiple evidence streams (*i.e.*, chemistry, fate, release and engineering, exposure, hazard), and the search and screening results to date are provided in Section 2.1. EPA is seeking public comment on this draft scope document and will consider additional information identified following publication of this draft scope document, as appropriate, in developing the final scope of the risk evaluation.

Conditions of Use: EPA plans to evaluate manufacturing (including importing); processing; distribution in commerce; industrial, commercial, and consumer uses; and disposal of D4 in the risk evaluation. D4 is manufactured (including imported) in the United States. The chemical is processed as a reactant; incorporated into a formulation, mixture, or reaction product; and incorporated into articles. The identified processing activities also include the repackaging and recycling of D4. D4 is primarily used to make other silicone chemicals and as an ingredient in consumer products regulated by the Federal Food, Drug, and Cosmetic Act (FFDCA). Commercial uses were identified including adhesives and sealants, automotive care products, paints and coatings, and other plastic and rubber products. Additional

consumer uses including adhesives and sealants, automotive care products, laundry and dishwashing products, paints and coatings, and other plastic and rubber products were also identified.

Some of these conditions of use 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 Chemical Data Reporting (CDR), published literature, and consultation with stakeholders for both uses currently in production and uses whose production may have ceased. 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 in June 2020. Section 2.2 provides additional details about the conditions of use within the scope of the risk evaluation.

Conceptual Model: The conceptual models for D4 are presented in Section 2.6. Conceptual models are graphical depictions of the actual or predicted relationships of conditions of use, exposure pathways (*e.g.*, media), exposure routes (*e.g.*, inhalation, dermal, oral), hazards, and receptors throughout the life cycle of a chemical substance or category of chemical substances. EPA plans to focus the risk evaluation for D4 on the following exposures, hazards, and receptors with the understanding that updates may be made in the final scope document after consideration of public comments and completion of the systematic review data collection phase.

- *Exposures (Pathways and Routes), PESS:* EPA plans to evaluate releases to the environment as well as human and environmental exposures resulting from the conditions of use of D4 that EPA plans to consider in the risk evaluation. Exposures for D4 are discussed in Section 2.3. Additional information gathered through systematic review searches will also inform expected exposures.

  In Section 2.6, EPA presents the conceptual models describing the identified exposures (pathways and routes), receptors, and hazards associated with the conditions of use of D4 within the scope of the risk evaluation.

  Preliminarily, EPA plans to evaluate the following human and environmental exposure pathways, routes, receptors, and PESS in the scope of the risk evaluation. However, EPA plans to consider comments received on this draft scope document and other reasonably available information when finalizing this scope document, and to adjust the exposure pathways, exposure routes, hazards, and PESS included in the final scope document as needed.

  - *Occupational exposure:* EPA plans to evaluate exposures to workers and occupational non-users (ONUs) via the inhalation route, including incidental ingestion of inhaled dust, and exposures to workers via the dermal route associated with the manufacturing, processing, use, and disposal of D4. EPA plans to analyze dermal exposure for workers and ONUs to mists and dust that deposit on surfaces.
  - *Consumer and bystander exposure:* EPA plans to evaluate inhalation, dermal, and oral exposure to D4 for consumers and bystanders from the use of adhesives and sealants, automotive care products, cleaning and furnishing care, fabric, textiles and leather materials not covered elsewhere, laundry and dishwashing products, paints and coatings, plastics and rubber products not covered elsewhere, and toys, playground and sporting equipment; and the direct contact and/or mouthing of products or articles containing D4 for consumers.
  - *General population exposures:* EPA plans to evaluate general population exposure to D4 via the oral route from drinking water, surface water, groundwater, soil, human milk, and

fish ingestion; via the inhalation route from ambient air; and via the dermal route from contact with drinking water, surface water, groundwater, and soil.
  - *PESS:* EPA plans to include children; women of reproductive age (*e.g.*, women who may be pregnant or breastfeeding); populations with elevated fish ingestion such as subsistence fishing, indigenous, and native populations; workers; ONUs; consumers; and bystanders as PESS in the risk evaluation (Section 2.5).
  - *Environmental exposure:* EPA plans to evaluate exposure to D4 for aquatic and terrestrial receptors.

- *Hazards:* Hazards for D4 are discussed in Section 2.4. EPA reviewed information from the SEHSC submission requesting EPA conduct the risk evaluation for D4 (Docket ID: EPA-HQ-OPPT-2018-0443-0004) in order to identify potential environmental and human health hazards for D4. EPA also considered reasonably available information identified through systematic review methods as outlined in Appendix A to determine the broad categories of environmental and human health hazard effects to be evaluated in the risk evaluation. EPA plans to evaluate the epidemiological and toxicological literature for D4 using revised evaluation strategies that are described in a draft systematic review protocol that EPA plans to release later this year for public comment and peer review.

  EPA plans to evaluate all potential environmental and human health hazard effects identified for D4 in Sections 2.4.1 and 2.4.2, respectively. The potential environmental hazard effects and related information identified through the data screening phase of the SEHSC submission and all other reasonably available information that EPA plans to consider for the risk evaluation for D4 include absorption, distribution, metabolism, and excretion (ADME), developmental, gastrointestinal, mortality, neurological, nutritional and metabolic, reproductive, and respiratory effects. Similarly, the potential human health hazard effects and related information for D4 that EPA plans to consider for the risk evaluation include: ADME, developmental, cancer, endocrine, gastrointestinal, hematological and immune, hepatic, mortality, neurological, nutritional and metabolic, ocular and sensory, physiologically based pharmacokinetic modeling (PBPK), renal, reproductive, respiratory, skin, and connective tissue.

Analysis Plan: The analysis plan for D4 is presented in Section 2.7. The analysis plan outlines the general science approaches that EPA plans to use for the various evidence streams (*i.e.*, chemistry, fate, release and engineering, exposure, hazard) supporting the risk evaluation. The analysis plan is based on EPA's knowledge of D4 to date, which includes a review of identified information as described in Section 2.1. EPA plans to consider new information submitted by the public. Should additional data or approaches become reasonably available, EPA may consider them for the risk evaluation.

Peer Review: The draft risk evaluation for D4 will be peer reviewed. Peer review will be conducted in accordance with relevant and applicable methods for chemical risk evaluations, including using EPA's Peer Review Handbook (U.S. EPA, 2015b) and other methods consistent with section 26 of TSCA (see 40 CFR 702.45).

1 INTRODUCTION

On March 19, 2020, EPA received a request through the SEHSC from Dow Silicones Corporation, Elkem Silicones USA Corporation, Evonik Corporation, Momentive Performance Materials, Shin-Etsu Silicones of America, Inc., and Wacker Chemical Corporation to conduct a risk evaluation for D4 (CASRN 556-67-2) (EPA-HQ-OPPT-2018-0443) under the Frank R. Lautenberg Chemical Safety for the 21st Century Act, the legislation that amended TSCA on June 22, 2016. On October 6, 2020, EPA notified the requesters that the Agency had granted their manufacturer requested risk evaluation for D4. Pursuant to 40 CFR 702.37(e)(6)(iv), the requesters had 30 days subsequent to receipt of this notification to withdraw their request. In November 2020, upon the expiration of this 30-day period, the risk evaluation for D4 was initiated.

Amended TSCA includes requirements and deadlines for actions related to conducting risk evaluations of existing chemicals, including requirements for manufacturer requested risk evaluations. TSCA section 6(b)(4) and 40 CFR 702.37 direct EPA to review manufacturer requests for risk evaluations on a chemical substance, and upon granting the request pursuant to 40 CFR 702.37, TSCA section 6(b)(4) directs EPA to initiate a risk evaluation on the chemical substance. TSCA section 6(b)(4)(A) directs EPA, in conducting risk evaluations for existing chemicals, 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."

TSCA section 6(b)(4)(D) and implementing regulations require that EPA publish the scope of the risk evaluation to be conducted, including the hazards, exposures, conditions of use, and PESS that the Administrator expects to consider, within 6 months after the initiation of a risk evaluation. In addition, a draft scope document is to be published pursuant to 40 CFR 702.41. This document presents for comment the draft scope of the risk evaluation to be conducted for D4.

2 SCOPE OF THE EVALUATION

2.1 Reasonably Available Information

EPA conducted a comprehensive search for reasonably available information[1] to support the development of this draft scope document for D4. EPA leveraged the data and information sources already identified in the SEHSC submission requesting that EPA conduct the risk evaluation for D4. (see Appendix A.4); any other data or information identified throughout the public comment period for the submission and EPA's review process for this manufacturer requested risk evaluation, as laid out in 40 CFR 702.37; as well as data and information sources submitted through an enforceable consent agreement (ECA) issued by EPA in 2014 requiring environmental monitoring data to help the Agency better understand the presence of this chemical in the environment (EPA-HQ-OPPT-2012-0209). In addition, EPA conducted an independent search for additional data and information on physical and chemical properties, environmental fate, engineering, exposure, environmental and human health hazards that could be obtained from the following general categories of sources:

1. Databases containing publicly available, peer-reviewed literature;
2. Gray literature, which is defined as the broad category of data/information sources not found in standard, peer-reviewed literature databases, including white papers, conference proceedings, technical reports, reference books, dissertations, information on various stakeholder websites, and other databases; or
3. Data and information submitted under TSCA sections 4, 5, 8(e), and 8(d), as well as "for your information" (FYI) submissions.

Search terms were used to search each of the literature streams and gather D4 studies. These terms and the methods used to develop them are listed in Appendix A. The studies resulting from the search process were loaded into the EPA Health and Environmental Research Online (HERO) database and prioritized for screening. Customized criteria (*e.g.*, keywords, positive and negative seed papers) were used to determine relevant literature for each of the disciplines: fate, physical and chemical properties, engineering, exposure, and hazard. Prioritized literature was then screened according to the population, exposure, setting/scenario, and outcome (PESO); and receptor, exposure setting/scenario, and outcome (RESO) statements listed in Appendix A. Literature that was not prioritized for any discipline is considered off-topic and excluded from further review. The screening process results are presented in the form of literature inventory trees and heat maps in Section 2.1.2. The screening process was conducted based on EPA's planning, execution, and assessment activities outlined in Appendix A.

In addition, 159 unique data and information sources identified by SEHSC in the manufacturer request submission (Docket ID: EPA-HQ-OPPT-2018-0443-0004) (see Appendix A.4) were not included in EPA's search results. The majority of these sources are comprised of industry studies, guidance documents, and documents of a more general nature that would not be captured by EPA's search strategy described in Appendix A.1. In some cases, sources were submitted for analogous chemicals, which were not part of the search terms used by EPA. EPA fully applies the same screening and evaluation methods to these additional references as applied to those sources identified by EPA.

[1] *Reasonably available information* means information that EPA possesses or can reasonably generate, obtain, and synthesize for use in risk evaluations, considering the deadlines specified in TSCA section 6(b)(4)(G) for completing such evaluation. Information that meets the terms of the preceding sentence is reasonably available information whether or not the information is confidential business information, that is protected from public disclosure under TSCA section 14 (40 CFR 702.33).

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

2.1.1 Search of Gray Literature

EPA surveyed the gray literature and identified 69 search results relevant to EPA's risk assessment needs for D4. Appendix A.3.4 lists the gray literature sources that yielded 69 discrete data or information sources relevant to D4. EPA further categorized the data and information into the various topic areas (or disciplines) supporting the risk evaluation (*e.g.*, physical chemistry, environmental fate, environmental hazard, human health hazard, exposure, engineering), and the breakdown is shown in Figure 2-1. EPA may refine and revise the numbers in Figure 2-1 following consideration of public comments and further evaluation using systematic review methods

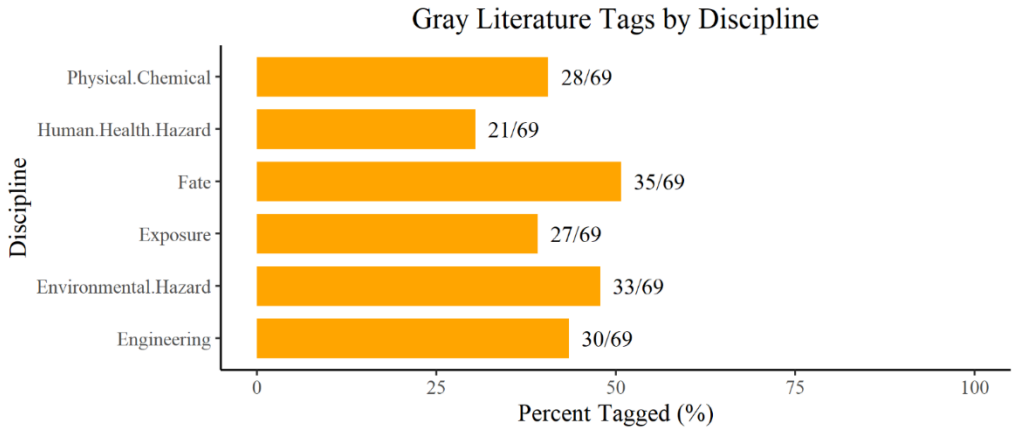

Figure 2-1. Gray Literature Tags by Discipline for D4

The percentages across disciplines do not add up to 100%, as each source may provide data or information for various topic areas (or disciplines). The gray literature sources depicted in this figure were those identified by EPA using systematic review methods outlined in Appendix A.3.

2.1.2 Search of Literature from Publicly Available Databases (Peer-Reviewed Literature)

EPA has conducted searching and screening of the reasonably available literature using the process outlined in Appendix A. This includes performing a comprehensive search of the reasonably available peer-reviewed literature on physical and chemical properties, environmental fate and transport, engineering (environmental release and occupational exposure), exposure (environmental, general population, and consumer) and environmental and human health hazards of D4 and four degradation products, octamethyltetrasiloxanediol (CASRN 3081-07-0), hexamethyltrisiloxanediol (CASRN 3663-50-1), tetramethyldisiloxanediol (CASRN 1118-15-6) and dimethylsilanediol (DMSD) (CASRN 1066-42-8) (see Section 2.3.2). Eligibility criteria were applied in the form of PECO, PESO, and RESO statements to all of the reasonably available information in all of the different information pools described in this subsection and in Section 2.1 above (see Appendix A). Included references met the PECO, PESO, and RESO criteria, whereas excluded references did not meet the criteria (*i.e.*, not relevant), and supplemental material was considered as potentially relevant (see Appendix A.2). EPA plans to evaluate the reasonably available information identified for each discipline during the development of the risk evaluation.

EPA created literature inventory trees to graphically illustrate the flow of data and information sources following full-text screening (see Figure 2-2, Figure 2-3, Figure 2-5, Figure 2-7, and Figure 2-9) for D4 and the four degradation products mentioned above. EPA used the Health Assessment Workplace Collaborative (HAWC) tool to develop web-based literature inventory trees illustrating, through interactive links, studies that were included or excluded. These literature inventory trees enhance the transparency of the decisions resulting from the screening process described in Appendix A. For each of the corresponding disciplines, the literature was tagged to be included for evaluation during the risk evaluation. Literature inventory trees for physical and chemical properties are provided as a static diagram (Figure 2-2). For all other disciplines, static screen captures are provided in addition to links within each figure's caption to the interactive trees. The links show individual studies that were tagged as included, excluded, or supplemental. Supplemental studies did not meet all inclusion criteria but may be considered during the risk evaluation as supporting information (see Appendix A). These studies can be accessed through the hyperlink provided in the associated caption below each figure. In some figures, the sum of the numbers for the various subcategories may be larger than the broader category because some studies may be included under multiple subcategories. In other cases, the sum of the various subcategories may be smaller than the main category because some studies may not be depicted in the subcategories if their relevance to the risk evaluation was unclear.

In addition, EPA tabulated the number and characteristics of the data and information sources included in the full-text screening process in the form of literature inventory heat maps for the fate, engineering, exposure, and hazard disciplines (see Figure 2-4, Figure 2-6, Figure 2-8, and Figure 2-10). For each of these four disciplines, a static image of the literature inventory heat map is provided, and a link to the interactive version presented in HAWC is included in the caption below each diagram.

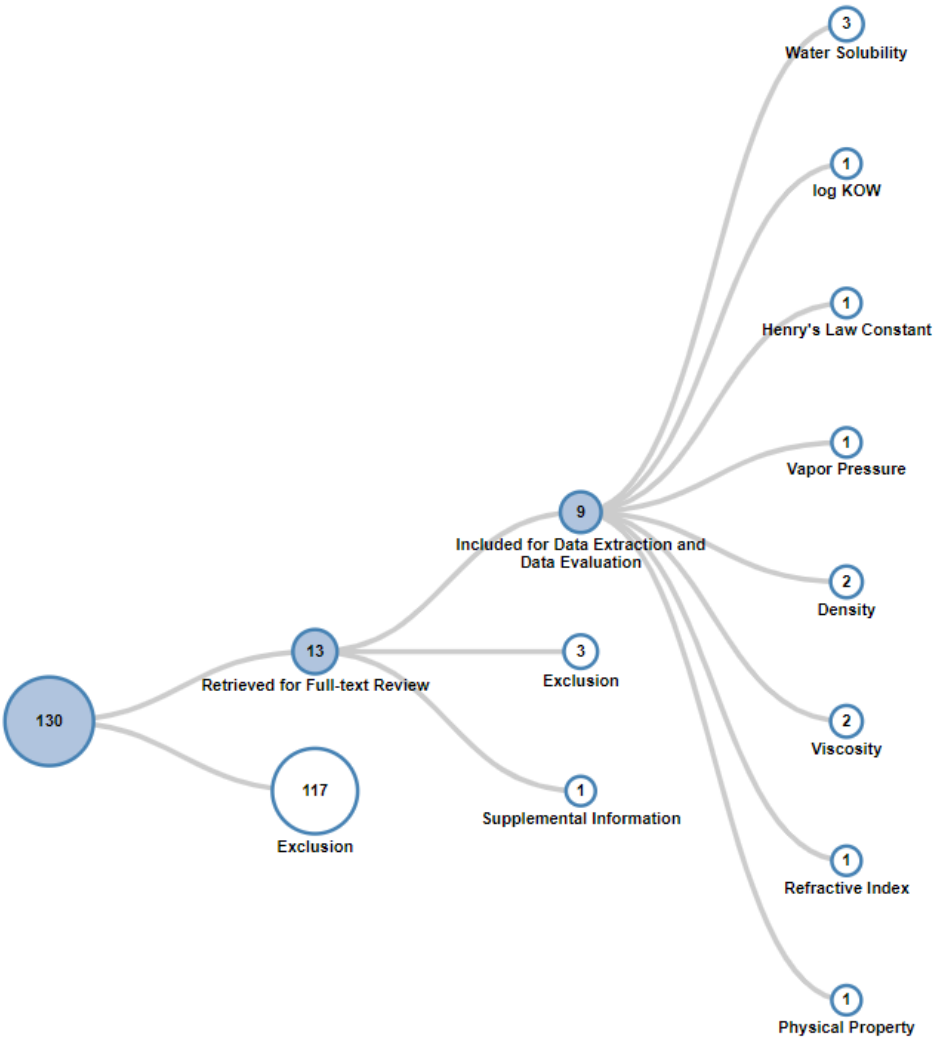

Figure 2-2. Peer-Reviewed Literature – Physical and Chemical Properties Search Results for D4
View the interactive literature inventory tree in HAWC. Data in this static figure represent references obtained from the publicly available databases search (see Appendix A.1.2) and from the SEHSC submission that were included during full-text screening as of May 6, 2021. Additional data may be added to the interactive version as they become available.

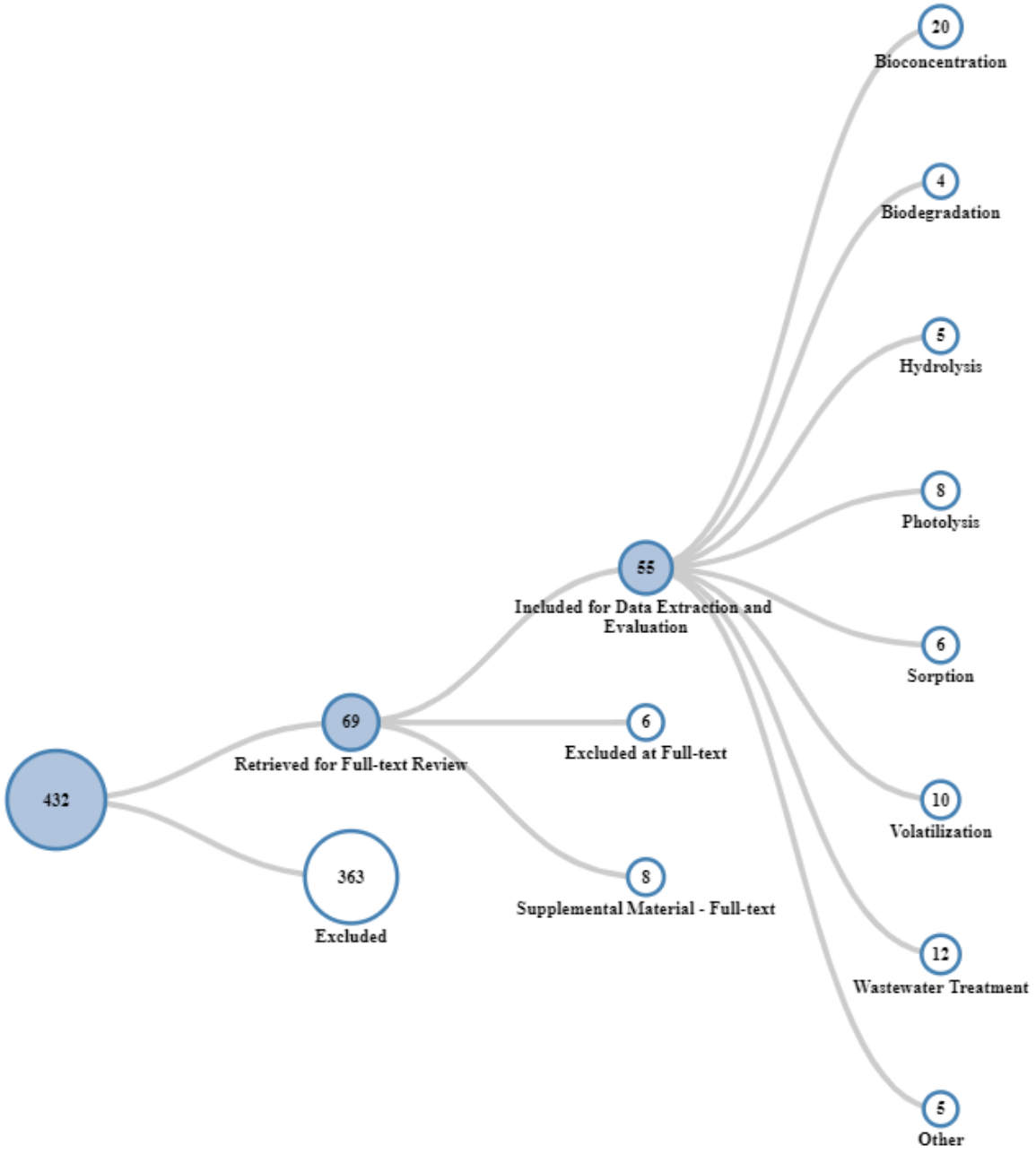

Figure 2-3. Peer-Reviewed Literature – Fate and Transport Search Results for D4
View the interactive literature inventory tree in HAWC. Data in this figure represent references obtained from the publicly available databases search (see Appendix A.1.2) and from the SEHSC submission that were included during full-text screening as of May 20, 2021. Additional data may be added to the interactive version as they become available.

	Media					
Endpoint	**Air**	**Soil, Sediment**	**Wastewater, Biosolids**	**Water**	**Other**	**Grand Total**
Bioconcentration	1	4	2	19	1	20
Biodegradation		1	1	2		4
Hydrolysis		2	1	2		5
Photolysis	7	2	1	1		8
Sorption		3	1	3		6
Volatilization	4	3	3	6		10
Wastewater Treatment	3	3	11	1		12
Other	2	3	1	4		5
Grand Total	14	15	14	30	1	55

Figure 2-4. Peer-Reviewed Literature Inventory Heat Map – Fate and Transport Search Results for D4

View the interactive version in HAWC for additional study details. The column totals, row totals, and grand totals indicate total numbers of unique references, as some references may be included in multiple cells. The various shades of color visually represent the number of relevant references identified by exposure media or data type. The darker the color, the more references are available for a given exposure media or data type. Data in this figure represent references obtained from the publicly available databases search (see Appendix A.1.2) and from the SEHSC submission that were included during full-text screening as of May 20, 2021. Additional data may be added to the interactive version as they become available.

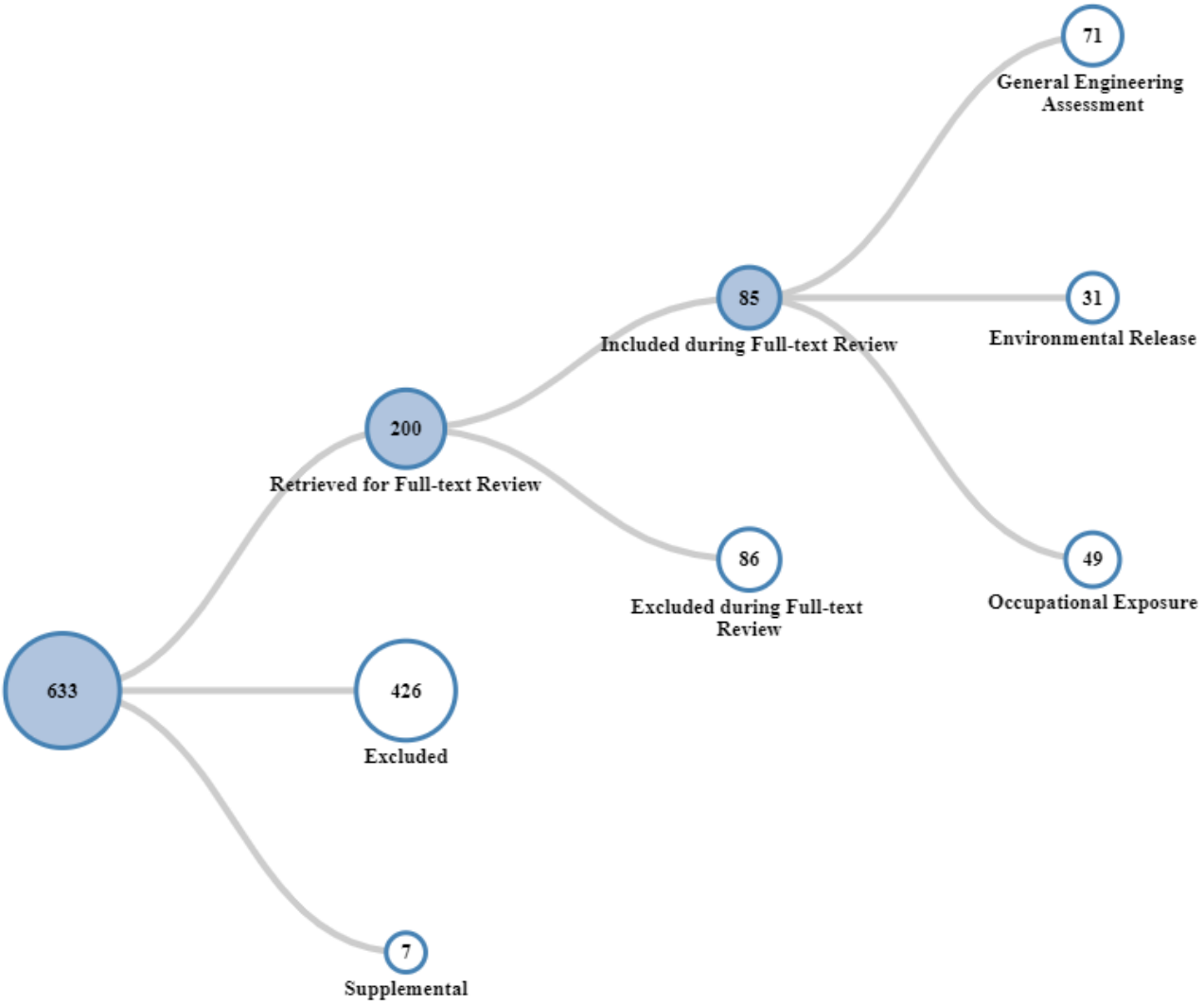

Figure 2-5. Peer-Reviewed Literature Inventory Tree – Engineering Search Results for D4
View the interactive literature inventory tree in HAWC. Data in this figure represents references obtained from the publicly available databases search (see Appendix A.1.2.) and from the SEHSC submission that were included during full-text screening as of May 6, 2021. Additional data may be added to the interactive version as they become available.

Data Type	Evidence Tags	
Environmental Releases	Description of release source	25
	No evidence tag	1
	Release frequency	2
	Release or emission factors	17
	Release quantity	8
	Waste treatment methods and pollution control	15
	Total	31
General Engineering Assessment	Chemical concentration	49
	Life cycle description	14
	No evidence tag	5
	Number of sites	7
	Process description	23
	Production, import, or use volume	22
	Throughput	7
	Total	71
Occupational Exposures	Area sampling data	27
	Dermal exposure data	18
	Engineering control	8
	Exposure duration	10
	Exposure frequency	6
	Exposure route	31
	No evidence tag	4
	Number of workers	12
	Particle size characterization	1
	Personal protective equipment	8
	Personal sampling data	7
	Physical form	21
	Worker activity description	14
	Total	49
Grand Total		85

Figure 2-6. Peer-Reviewed Literature Inventory Heat Map – Engineering Search Results for D4
View the interactive version in HAWC for additional study details. Data in this figure represent references obtained from the publicly available databases search (see Appendix A.1.2) and from the SEHSC submission that were included during full-text screening as of May 6, 2021. Additional data may be added to the interactive version as they become available.

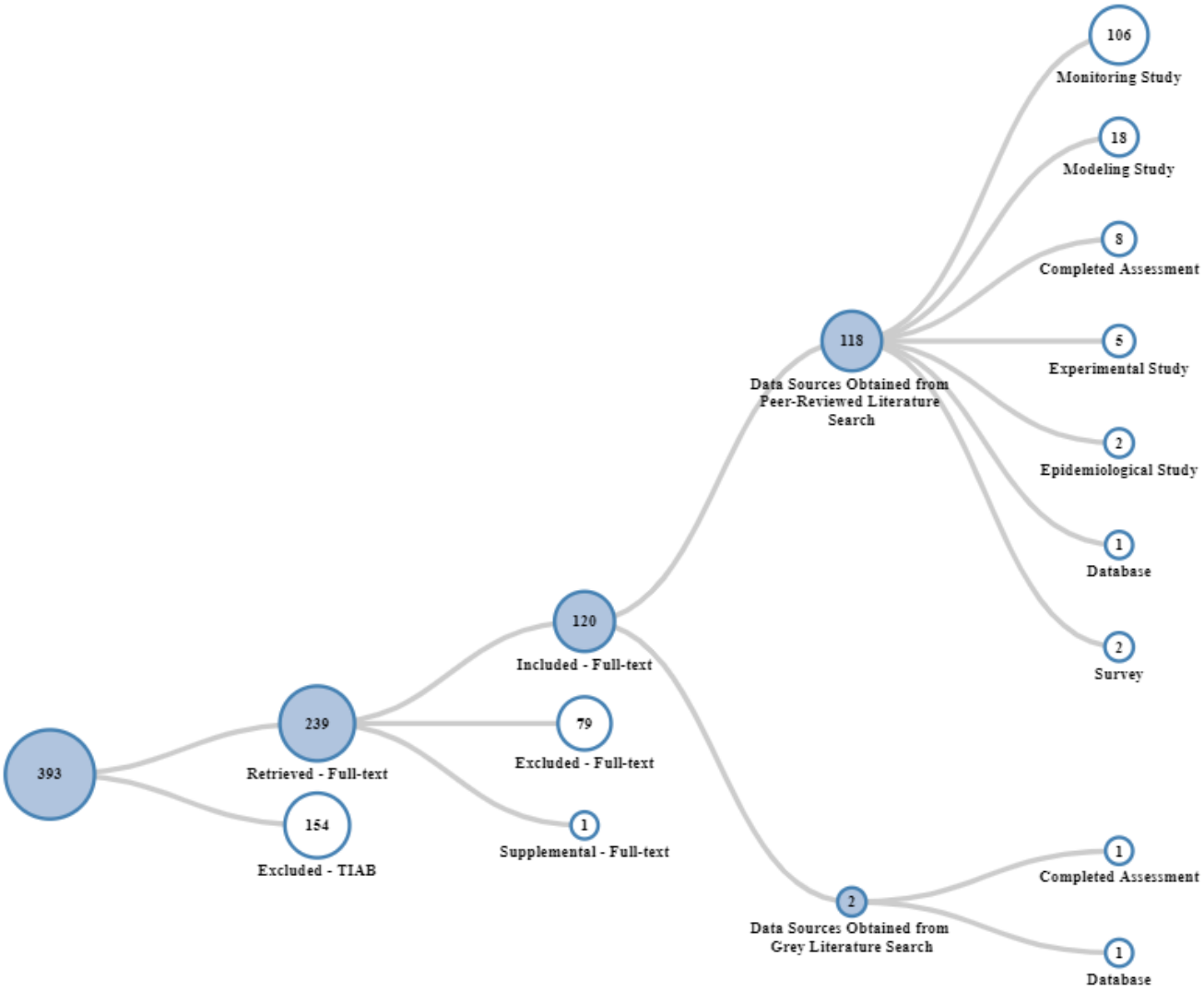

Figure 2-7. Peer-Reviewed Literature and Gray Literature – Exposure Search Results for D4
View the interactive literature inventory tree in HAWC. Data in this figure represents references obtained from the publicly available database searches (see Appendix A.1.2.); gray literature reference searches (see Appendix A.3); and from the SEHSC submission that were included during full-text screening as of May 5, 2021. Additional data may be added to the interactive version as they become available.

	Data Type							
Media (group)	**Monitoring Study**	**Modeling Study**	**Completed Assessment**	**Experimental Study**	**Epidemiological Study**	**Database**	**Survey**	**Grand Total**
Ambient Air	29	8	2	2	1			32
Biosolids/Sludge	15	2	4					18
Drinking Water			1					1
Groundwater	1							1
Sediment	28	3	4					29
Soil	14	4	3	1	2		1	17
Surface Water	16	5	4					20
Wastewater	24	3	4					27
Aquatic Species	31		3		1		1	33
Terrestrial Species	5		1		2		1	6
Consumer	10	3	4	5		1		16
Dietary	1		1					2
Dust	7	1	1					8
Exposure Factors			1					1
Exposure Pathway	6	3	1					8
Human Biomonitoring	8	3	1	2				13
Indoor Air	13	2	1	2				15
Isomers	9			1		1	1	9
Use Information			2			1		3
No Evidence Type			1					1
Land Disposal/Landfill	3	1						3
Grand Total	106	18	9	5	2	2	2	120

Figure 2-8. Peer-Reviewed and Gray Literature Inventory Heat Map –Exposure – Search Results for D4

View the interactive version in HAWC for additional study details. The column totals, row totals, and grand totals indicate total numbers of unique references only, as some references may be included in multiple cells. The various shades of color visually represent the number of relevant references identified by exposure media or data type. The darker the color, the more references are available for a given exposure media or data type. Data in this figure represent references obtained from the publicly available database searches (see Appendix A.1.2); gray literature reference searches (see Appendix A.3); and from the SEHSC submission that were included during full-text screening as of May 5, 2021. Additional data may be added to the interactive version as they become available.

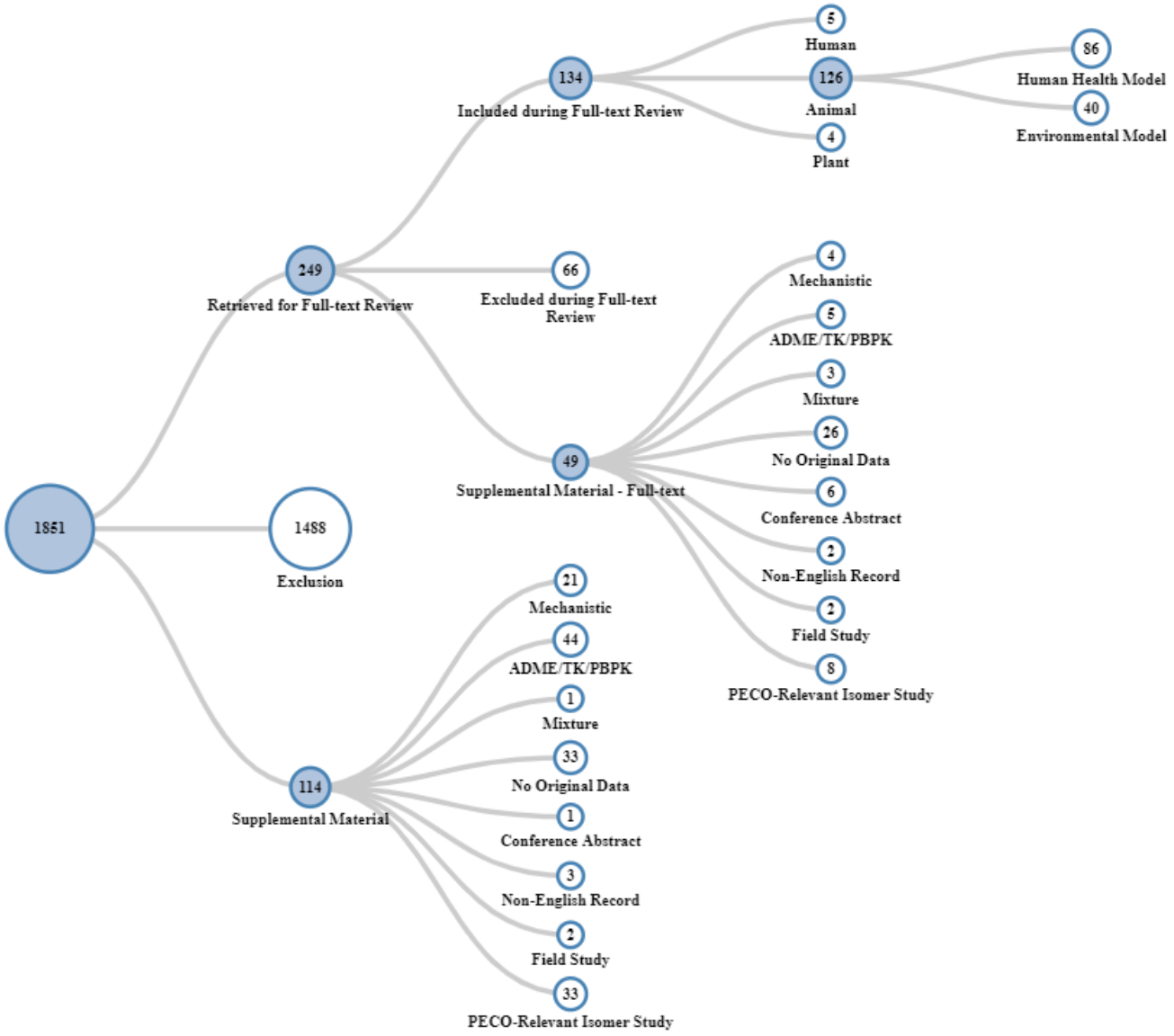

Figure 2-9. Peer-Reviewed Literature Inventory Tree – Human Health and Environmental Hazards Search Results for D4

View the interactive literature inventory tree in HAWC. Data in this figure represent references obtained from the publicly available database searches (see Appendix A.1.2) and from the SEHSC submission that were included during full-text screening as of May 6, 2021. Additional data may be added to the interactive version as they become available.

	Evidence Type				
Health Outcomes	**Human**	**Animal - Human Health Model**	**Animal - Environmental Model**	**Plant**	**Grand Total**
ADME		47	3		50
Cancer		3			3
Cardiovascular					
Developmental		19	4	1	24
Endocrine		13			13
Gastrointestinal	1	2	1		4
Hematological and Immune	2	10			12
Hepatic		15			15
Mortality		3	5		8
Musculoskeletal					
Neurological		5	2		7
Nutritional and Metabolic		6	4		10
Ocular and Sensory	2	5			7
PBPK					
Renal		3			3
Reproductive		22	2		24
Respiratory	1	43	1		45
Skin and Connective Tissue	1	6			7
No Tag	1	21	29	3	53
Grand Total	5	86	40	4	134

Figure 2-10. Peer-Reviewed Literature Inventory Heat Map – Human Health and Environmental Hazards Search Results for D4

View the interactive version in HAWC for additional study details. The numbers indicate the number of studies with title and abstract keywords related to a particular health outcome, not the number of studies that observed an association with D4. Evidence types were manually extracted, and health outcomes were determined via machine learning. Therefore, in studies examining multiple health outcomes and evidence types, the connections between health outcome, and evidence type may not be accurately represented. If a study evaluated multiple health outcomes or included multiple populations or study designs, it is shown here multiple times. Data in this figure represent references obtained from the publicly available database searches (see Appendix A.1.2) and those from the SEHSC submission that were included during full-text screening as of May 6, 2021.

2.1.3 Search of TSCA Submissions

Table 2-1 presents the results of screening the titles of data sources and reports submitted to EPA under various sections of TSCA for D4 and the four degradation products identified in Section 2.1.2. EPA screened a total of 576 submissions[2] using PECO or other statements that identify inclusion/exclusion criteria specific to individual disciplines (see Table 2-1 for the list of disciplines). The details about the criteria are presented in Appendix A.2.1. EPA identified 186 submissions that met the inclusion criteria in these statements and identified 145 submissions with supplemental data. EPA excluded 245 submissions because they were identified as one of the following:

- Draft report or preliminary results of a final report included based on screening criteria

[2] Of the 576 submissions, 565 were for D4, three of which also included information on the degradation products. An additional 11 submissions were for the degradation products only.

- Duplicate or summary of a report received in another submission that was included based on screening criteria
- Published report or draft manuscript for publication, which will be checked against results of the peer or other gray literature searches
- Letter, memo, or notification containing no data
- Study amendment containing no data
- Submission on a different chemical not in scope
- Request for an extension or modification
- Development and/or details of a test method or test protocol
- Economic impact analysis
- Type of study that did not meet the screening criteria:
    - Study measuring biochemical oxygen demand
    - Study measuring water solubility in the presence of humic acid
    - Measurement of exposure concentrations resulting from a chemical spill
    - Measurement of exposure due to food processing components, medications, or use of anti-perspirants
    - Study examining effects on ozone

Table 2-1. Results of Title Screening of Submissions to EPA under Various Sections of TSCA

Discipline	Included		Supplemental[a]	
	D4	Degradants	D4	Degradants
Physical and Chemical Properties	15	0	0	0
Environmental Fate and Transport[b]	36	4	0	0
Environmental and General Population Exposure	13	1	0	0
Occupational Exposure/Release Information	10	1	0	0
Environmental Hazard[b]	45	3	17	0
Human Health Hazard	88	3	127	1

Individual submissions may be relevant to multiple disciplines, and so column totals may be higher than 186.
[a] Included submissions may contain supplemental data for other disciplines, which will be identified at full-text review.
[b] One submission met the inclusion criteria for both D4 and for the degradation products.

2.2 Conditions of Use

The SEHSC submission requesting that EPA conduct a risk evaluation of D4 included a list of circumstances that EPA has since determined to be conditions of use[3] that warrant inclusion in the risk evaluation for this chemical substance, pursuant to TSCA section 3(4). Following the submission of the request for a risk evaluation of D4, EPA further assembled reasonably available information from CDR to identify additional conditions of use for inclusion in this scope of the risk evaluation. EPA consulted a variety of other sources (including published literature, company websites, and government and commercial trade databases and publications) to identify uses of D4. To identify formulated products containing D4, EPA searched for safety data sheets (SDS) using internet searches, EPA Chemical and Product Categories (CPCat) (U.S. EPA, 2019) data, and other resources in which SDSs could be found. SDSs were cross-checked with company websites to make sure that each product SDS was current. In addition, EPA incorporated communications with companies, industry groups, and public comments to supplement the use information. 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 in June 2020. The October 6, 2020 notification in which EPA granted the request for a risk evaluation for D4 identified additional conditions of use that EPA plans to include in the risk evaluation.

The categories and subcategories of conditions of use that EPA plans to consider in the risk evaluation are presented in Section 2.2.1 (Table 2-2). The conditions of use included in the scope of the risk evaluation are those reflected in the life cycle diagrams and conceptual models.

The circumstances on which SEHSC requested that EPA conduct a risk evaluation of D4 were determined to be conditions of use. After gathering reasonably available information related to the manufacture, processing, distribution in commerce, use, and disposal of D4, EPA also identified those activities for D4 the Agency determined not to be conditions of use. These excluded activities are described in Section 2.2.2.

2.2.1 Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

Table 2-2 lists the conditions of use that are included in the scope of the risk evaluation.

Table 2-2. Categories and Subcategories of Conditions of Use Included in the Scope of the Risk Evaluation

Life Cycle Stage[a]	Category[b]	Subcategory[c]	References
Manufacturing	Manufacturing[d]		U.S. EPA (2020a)
	Importing		U.S. EPA (2020a)
Processing	Processing as a reactant	Adhesives and sealant chemicals[d]	U.S. EPA (2020a)
		All other basic inorganic chemical manufacturing[d]	U.S. EPA (2020a)

[3] *Conditions of use* means the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of (15 U.S.C. 2602(4)).

Life Cycle Stage[a]	Category[b]	Subcategory[c]	References
Processing		All other basic organic chemical manufacturing[d]	U.S. EPA (2020a)
		All other chemical product and preparation manufacturing[d]	U.S. EPA (2020a)
		Plastic material and resin manufacturing[d]	EPA-HQ-OPPT-2018-0443-0004
		Synthetic rubber manufacturing[d]	EPA-HQ-OPPT-2018-0443-0004
	Incorporation into formulation, mixture, or reaction product	All other basic inorganic chemical manufacturing[d]	U.S. EPA (2020a)
		All other chemical product and preparation manufacturing[d]	U.S. EPA (2020a)
		Asphalt paving, roofing, and coating materials manufacturing	U.S. EPA (2020a)
		Computer and electronic product manufacturing	U.S. EPA (2020a)
		Cyclic crude and intermediate manufacturing	U.S. EPA (2020a)
		Electrical equipment, appliance, and component manufacturing	U.S. EPA (2020a)
		Miscellaneous manufacturing[d]	EPA-HQ-OPPT-2018-0443-0004
		Paint and coating manufacturing[d]	EPA-HQ-OPPT-2018-0443-0004
		Rubber product manufacturing	U.S. EPA (2020a)
		Synthetic rubber manufacturing	U.S. EPA (2020a)

Life Cycle Stage[a]	Category[b]	Subcategory[c]	References
Processing	Processing – repackaging	All other basic inorganic chemical manufacturing	U.S. EPA (2020a)
		All other chemical product and preparation manufacturing	U.S. EPA (2020a)
		Miscellaneous manufacturing	U.S. EPA (2020a)
Distribution in commerce	Distribution in commerce		
Commercial uses	Adhesives and sealants	Adhesives and sealants[d]	U.S. EPA (2020a)
	Automotive care products	Automotive care products[d]	U.S. EPA (2020a)
	Furnishing, cleaning, treatment/care products	Fabric, textile, and leather products not covered elsewhere[d]	EPA-HQ-OPPT-2018-0443-0004
		Cleaning and furnishing care products[d]	U.S. EPA (2020a)
	Ink, toner, and colorant products	Ink, Toner, and Colorant Products	3M (2018) 3M (2019)
	Laboratory chemicals	Laboratory chemicals[d]	EPA-HQ-OPPT-2018-0443-0004
	Paints and coatings	Paints and coatings[d]	U.S. EPA (2020a)
	Plastic and rubber products not covered elsewhere	Plastic and rubber products not covered elsewhere[d]	U.S. EPA (2020a)
	Other	Animal grooming products	EPA-HQ-OPPT-2018-0443-0016
Consumer uses	Adhesives and sealants	Adhesives and sealants[d]	EPA-HQ-OPPT-2018-0443-0004
	Automotive care products	Automotive care products[d]	EPA-HQ-OPPT-2018-0443-0004
	Furnishing, cleaning, treatment/care products	Cleaning and furnishing care products[d]	EPA-HQ-OPPT-2018-0443-0004
		Fabric, textile, and leather products not covered elsewhere[d]	EPA-HQ-OPPT-2018-0443-0004

Life Cycle Stage[a]	Category[b]	Subcategory[c]	References
		Laundry and dishwashing products[d]	EPA-HQ-OPPT-2018-0443-0004
	Packaging, paper, plastic, hobby products	Plastic and rubber products not covered elsewhere[d]	U.S. EPA (2020a)
		Toys, Playground, and Sporting Equipment[d]	EPA-HQ-OPPT-2018-0443-0004
	Paints and coatings	Paints and coatings[d]	U.S. EPA (2020a)
	Other	Animal grooming products	Warren London (2019)
Disposal	Disposal		

[a] Life Cycle Stage Use Definitions (40 CFR 711.3)
- "Industrial use" means use at a site at which one or more chemicals or mixtures are manufactured (including imported) or processed.
- "Commercial use" means the use of a chemical or a mixture containing a chemical (including as part of an article) in a commercial enterprise providing saleable goods or services.
- "Consumer use" means the use of a chemical or a mixture containing a chemical (including as part of an article, such as furniture or clothing) when sold to or made available to consumers for their use.
- Although EPA has identified both industrial and commercial uses here for purposes of distinguishing scenarios in this document, the Agency interprets the authority over "any manner or method of commercial use" under TSCA section 6(a)(5) to reach both.

[b] These categories of conditions of use appear in the Life Cycle Diagram, reflect CDR codes, and broadly represent conditions of use of D4 in industrial and/or commercial settings.
[c] These subcategories reflect more specific conditions of use of D4.
[d] Circumstances on which SEHSC is requesting that EPA conduct a risk evaluation of D4.

2.2.2 Activities Excluded from the Scope of the Risk Evaluation

TSCA section 6(b)(4)(D) requires EPA to identify the hazards, exposures, conditions of use, and the PESS the Administrator expects to consider in a risk evaluation. TSCA section 3(4) also grants EPA discretion to determine the circumstances that are appropriately considered to be conditions of use for a particular chemical substance.[4] As a result, EPA does not plan to include in this scope or in the risk evaluation activities described below that the Agency does not consider to be conditions of use.

[4] *Chemical substance* means any organic or inorganic substance of a particular molecular identity, including any combination of such substances occurring in whole or in part as a result of a chemical reaction or occurring in nature, and any element or uncombined radical. Chemical substance does not include (1) any mixture; (2) any pesticide (as defined in the Federal Insecticide, Fungicide, and Rodenticide Act) when manufactured, processed, or distributed in commerce for use as a pesticide; (3) tobacco or any tobacco product; (4) any source material, special nuclear material, or byproduct material (as such terms are defined in the Atomic Energy Act of 1954 and regulations issued under such Act); (5) any article the sale of which is subject to the tax imposed by section 4181 of the Internal Revenue Code of 1954 (determined without regard to any exemptions from such tax provided by section 4182 or 4221 or any other provision of such Code); and (6) 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)).

TSCA section 3(2) also excludes from the definition of "chemical substance" "any food, food additive, drug, cosmetic, or device (as such terms are defined in section 201 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 321]) when manufactured, processed, or distributed in commerce for use as a food, food additive, drug, cosmetic, or device" as well as "any pesticide (as defined in the Federal Insecticide, Fungicide, and Rodenticide Act [7 U.S.C. 136 et seq.]) when manufactured, processed, or distributed in commerce for use as a pesticide." EPA has determined that the following uses of D4 are non-TSCA uses:

- The Food and Drug Administration lists D4 as an optional substance to be used in food packaging materials. Food packaging materials meet the definition for a "food additive" described in section 201 of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 321. Therefore, the use of D4 in food packaging materials is excluded from the definition of "chemical substance" in TSCA section 3(2)(B)(vi) and is not included in Table 2-2. Activities and releases associated with the use of such food packaging materials are therefore not "conditions of use" (defined as circumstances associated with "a chemical substance," TSCA section 3(4)) and will not be evaluated during risk evaluation.
- EPA determined that D4 is used in dental bonding agents and breast implants which meets the definition of "device" under section 201 of the FFDCA, 21 U.S.C. 321. Therefore, these uses are excluded from the definition of "chemical substance" in TSCA section 3(2)(B)(vi) and are not included in Table 2-2. Activities and releases associated with the use of such medical devices are therefore not "conditions of use" (defined as circumstances associated with "a chemical substance," TSCA section 3(4)) and will not be evaluated during risk evaluation.
- EPA determined that D4 is used in personal care products that meet the definition of "cosmetics" under section 201 of the FFDCA, 21 U.S.C. 321. Therefore, these uses are excluded from the definition of "chemical substance" in TSCA section 3(2)(B)(vi) and are not included in Table 2-2. Activities and releases associated with the use of such personal care products are therefore not "conditions of use" (defined as circumstances associated with "a chemical substance," TSCA section 3(4)) and will not be evaluated during risk evaluation.
- EPA determined that D4 is used in the over-the-counter medication which meets the definition of a "drug" in section 201 of the FFDCA, 21 U.S.C. 321. Therefore, the uses are excluded from the definition of "chemical substance" in TSCA section 3(2)(B)(vi) and are not included in Table 2-2. Activities and releases associated with the use of medical devices are not "conditions of use" (defined as circumstances associated with "a chemical substance," TSCA section 3(4)) and will not be evaluated during risk evaluation.

As described in the preamble to the Risk Evaluation Rule (*See Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act*, 33726 Fed. Reg. 33735 (July 20, 2017), EPA may consider potential risk from non-TSCA uses in evaluating whether a chemical substance presents an unreasonable risk. Although EPA would not regulate non-TSCA uses, 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).

2.2.3 Production Volume

As reported to EPA during the 2016 CDR reporting period and described here as a range to protect production volumes that were claimed as confidential business information (CBI), total production volume of D4 in 2015 was between 750 million and 1 billion pounds (U.S. EPA, 2020a). EPA plans to

include more recent production volume information from the 2020 CDR reporting period in the risk evaluation to support the exposure assessment.

2.2.4 Overview of Conditions of Use and Life Cycle Diagram

Figure 2-11 provides the life cycle diagram for D4. The life cycle diagram is a graphical representation of the various life stages of the industrial, commercial, and consumer use categories included within the scope of the risk evaluation. The information in the life cycle diagram is grouped according to the CDR processing codes and use categories (including functional use codes for industrial uses and product categories for commercial and consumer uses). Appendix E contains additional descriptions (*e.g.*, process descriptions, worker activities, process flow diagrams) for each manufacture, processing, distribution in commerce, use, and disposal category.

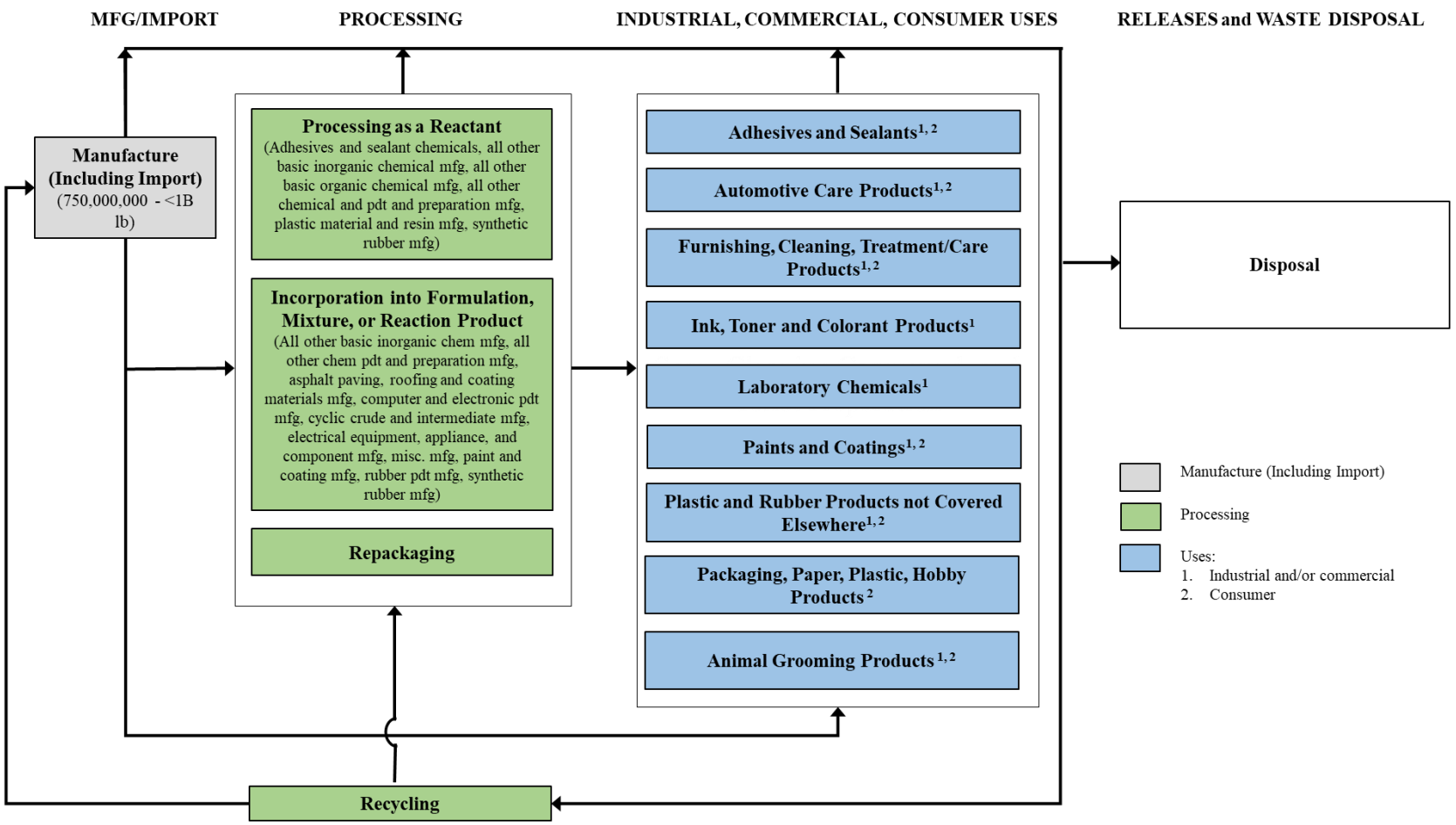

Figure 2-11. D4 Life Cycle Diagram

Distribution in commerce not included in LCD: For the purposes of the risk evaluation, distribution in commerce is the transportation associated with moving chemical substances in commerce. Unloading and loading activities are associated with other conditions of use. EPA assumes transportation of D4 is in compliance with existing regulations for the transportation of hazardous materials, and emissions are therefore minimal (with the exception of spills and leaks, which are outside the scope of the risk evaluation).

2.3 Exposures

For TSCA exposure assessments, EPA plans to analyze human and environmental exposures and releases to the environment resulting from the conditions of use within the scope of the risk evaluation of D4. In this section, the physical and chemical properties, environmental fate and transport properties and releases to the environment are described in addition to potential human and environmental exposures from TSCA conditions of use and from other possible or known sources. Release pathways and routes will be described in Section 2.6 to characterize the relationship or connection between the conditions of use of the chemical and the exposure to human receptors, including PESS, and environmental receptors. EPA plans to consider, where relevant, the duration, intensity (concentration), frequency and number of exposures in characterizing exposures to D4.

2.3.1 Physical and Chemical Properties

Consideration of physical and chemical properties is essential for a thorough understanding or prediction of environmental fate (*i.e.*, transport and transformation) and the eventual environmental concentrations. It can also inform the hazard assessment. Table 2-3 summarizes the physical and chemical property values preliminarily selected for use in the risk evaluation from among the range of reported values collected as of January 2021. This table may be updated as EPA continues to evaluate and integrate additional information through systematic review methods. EPA plans to use the physical and chemical characteristics identified through systematic review and provided in the SEHSC submission (Docket ID: EPA-HQ-OPPT-2018-0443). Figure 2-12 summarizes the distribution of reported values for eight physical and chemical properties routinely used in existing chemical risk evaluations. Appendix B presents summary statistics for reported physical and chemical property values. All physical and chemical property values that were extracted and evaluated as of July 2021 are presented in the supplemental file *Data Extraction and Data Evaluation Tables for Physical and Chemical Property Studies*.

Table 2-3. Physical and Chemical Properties for D4

Property or Endpoint	Value[a]	Reference	Data Quality Rating
Molecular formula	$C_8H_{24}O_4Si_4$	NA	NA
Molecular weight	296.61 g/mol	NA	NA
Physical state	Oily Liquid	(O'Neil, 2013)	High
Physical properties	Colorless Liquid	(RSC, 2020)	High
Melting point	17.5 °C	(O'Neil, 2013)	High
Boiling point	175 °C	(O'Neil, 2013)	High
Density	0.95603 g/cm^3 at 20 °C	(Zhang et al., 2015)	High
Vapor pressure	1.05 mm Hg at 25 °C	(NLM, 2020)	High

Property or Endpoint	Value[a]	Reference	Data Quality Rating
Vapor density	No data identified	–	–
Water solubility	0.056 mg/L at 23 °C	(Varaprath et al., 1996)	High
Log Octanol/water partition coefficient (Log Kow)	6.59 at 5.7 °C 6.98 at 21.7 °C 7.13 at 34.8 °C	Xu and Kropscott (2012) and Xu and Kropscott (2014)	High
Henry's Law constant (atm m^3/mol)	1.4 at 5.7 °C 11.8 at 21.7 °C 31.1 at 34.8 °C	Xu and Kropscott (2012) and Xu and Kropscott (2014)	High
Flash point	55 °C	(NLM, 2020)	High
Auto flammability	No data identified	–	–
Viscosity	2.30 cP at 25 °C	(NLM, 2020)	High
Refractive index	1.39674 at 20 °C	(Zhang et al., 2015)	High
Dielectric constant	2.4–2.405 at 20 °C	(Elsevier, 2019)	High
[a] Measured unless otherwise noted.			

Figure 2-12 displays a summary of the data collected by EPA during its independent systematic review process as of January 2021 for eight physical and chemical values routinely used in TSCA existing chemical risk evaluations. The box and whisker plots for each endpoint illustrate the mean (average, indicated by the blue diamond) and the 10th, 25th, 50th (median), 75th, and 90th percentiles. All individual data points are indicated by black squares, and value preliminarily selected for use in the risk evaluation is overlaid (indicated by the orange circle) to provide context for where it lies within the distribution of the data set. The number of unique primary data sources is indicated below each box and whisker plot. If multiple sources presented equivalent values and cited the same primary source, only one of those was included in the statistical calculations. As a result, the number of sources listed in Figure 2-12 may differ from the total number of data sources presented in Figure 2-2.

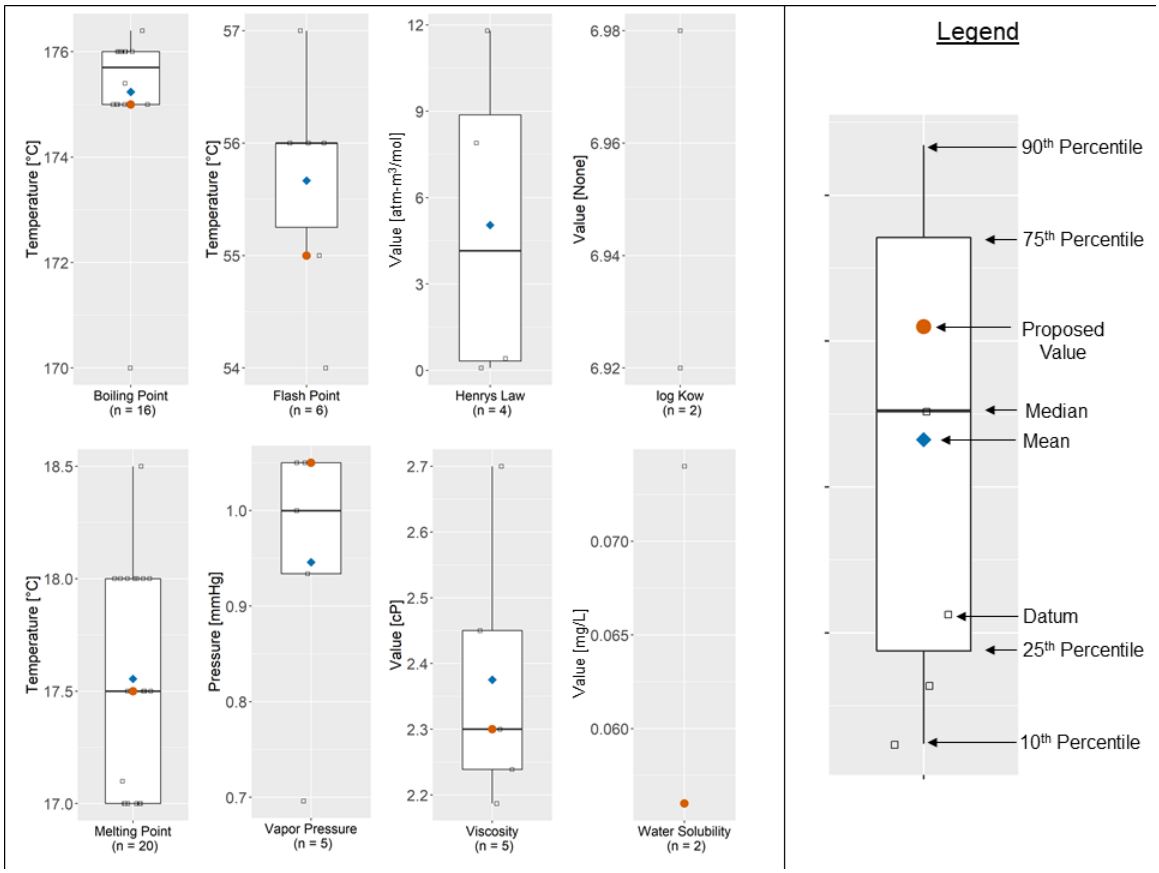

Figure 2-12. Box and Whisker Plots of Reported Physical and Chemical Property Values[5]

2.3.2 Environmental Fate and Transport

Understanding of environmental fate and transport processes assists in the determination of the specific exposure pathways and potential human and environmental receptors that need to be assessed in the risk evaluation for D4. EPA plans to use the environmental fate characteristics described in Appendix C to support the development of 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 in the SEHSC submission (Docket ID: EPA-HQ-OPPT-2018-0443).

D4 undergoes abiotic ring opening in water, soil, and sediment to form octamethyltetrasiloxanediol (CASRN 3081-07-0), which subsequently undergoes step-wise abiotic degradation through hexamethyltrisiloxanediol (CASRN 3663-50-1) and tetramethyldisiloxanediol (CASRN 1118-15-6) into the stable end-product dimethylsilanediol (DMSD) (CASRN 1066-42-8) (Xu and Miller, 2008; Durham, 2005; Xu, 1999). Studies have reported that DMSD aerobically biodegrades in soil into orthosilicic acid (CASRN 10193-36-9) under specific field and laboratory conditions (Sabourin et al., 1996; Lehmann et al., 1998; Sabourin et al., 1999). However, the reported rates of DMSD degradation were slow enough that DMSD has been detected in environmental samples (Lehmann et al., 2000; Xu, 2019; Fendinger et al., 1997) (TSCA section 8(e) submission 8EHQ-16-20460).

Based on this, EPA is requesting information from the public on the environmental fate characteristics of octamethyltetrasiloxanediol (CASRN 3081-07-0), hexamethyltrisiloxanediol (CASRN 3663-50-1),

[5] These values may be updated as EPA continues to evaluate and integrate additional information through systematic review and provided in the SEHSC submission (Docket ID: EPA-HQ-OPPT-2018-0443).

tetramethyldisiloxanediol (CASRN 118-15-6), DMSD (CASRN 1066-42-8), and orthosilicic acid (CASRN 10193-36-9). Physical and chemical property values for these substances, except orthosilicic acid, were extracted and evaluated as of July 2021 and are presented in the supplemental file *Data Extraction and Data Evaluation Tables for Physical and Chemical Property Studies for D4 Degradants*. However, EPA recognizes that only DMSD has been detected in environmental samples and that orthosilicic acid (CASRN 10193-36-9) is a macroelement originating from silicate minerals in soil and marine environments.

2.3.3 Releases to the Environment

Releases to the environment from conditions of use are a component of potential exposure and may be derived from reported data that are obtained through direct measurement, calculations based on empirical data and/or assumptions and models.

D4 is not reported to the Toxics Release Inventory (TRI). There may be releases of D4 from industrial sites to wastewater treatment plants (WWTP), surface water, air, and landfill. Articles that contain D4 may release D4 to the environment during use or through recycling and disposal. EPA plans to review these data in conducting the exposure assessment component of the risk evaluation for D4.

2.3.4 Environmental Exposures

The manufacturing, processing, distribution, use, and disposal of D4 can result in releases to the environment and exposure to aquatic and terrestrial receptors (biota). Environmental exposures are informed by releases into the environment, overall persistence, degradation, and bioaccumulation within the environment, and partitioning across different media. Concentrations of chemical substances in biota provide evidence of exposure. EPA plans to review reasonably available environmental monitoring data for D4.

As described in Section 2.3.2, 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 information for environmental exposure to D4 degradants. Therefore, EPA is requesting information from the public on the environmental concentration of DMSD and the intermediate degradation products of D4 in water, soil, and sediment.

2.3.5 Occupational Exposures

EPA plans to evaluate worker activities where there is a potential for exposure under the various conditions of use (distribution in commerce, manufacturing, processing, industrial/commercial uses, and disposal) described in Section 2.2. In addition, EPA plans to evaluate exposure to occupational non-users (ONUs), *i.e.*, workers who do not directly handle the chemical but perform work in an area where the chemical is present. EPA will not make risk determinations based on assumptions about the use of personal protective equipment (PPE) or control technologies. However, EPA plans to develop exposure scenarios with and without the use of PPE and engineering controls to inform any potential risk management required subsequent to an unreasonable risk determination for workers or ONUs.

Examples of worker activities associated with the conditions of use within the scope of the risk evaluation for D4 that EPA may analyze include, but are not limited to:

- Unloading and transferring D4 to and from storage containers to process vessels;
- Handling, transporting, and disposing of waste containing D4;
- Cleaning and maintaining equipment;

- Sampling chemicals, formulations or products containing D4 for quality control;
- Repackaging chemicals, formulations or products containing D4; and
- Perform other work activities in or near areas where D4 is used.

D4 is a liquid at room temperature and, as stated in Table 2-3, has a vapor pressure of 1.05 mm Hg at 25 °C. Because the chemical is semi-volatile, EPA plans to analyze inhalation exposure to vapor for workers and ONUs. EPA also plans to analyze inhalation exposure for workers and ONUs in occupational scenarios where D4 or products containing D4 are applied via spray application methods or are handled as a dry powder. D4 does not have occupational exposure limits established by the Occupational Health and Safety Administration (OSHA), the National Institute for Occupational Safety and Health (NIOSH), or the American Conference of Governmental Industrial Hygienists (ACGIH).

Based on the conditions of use, EPA plans to analyze worker exposure to liquids and/or solids via the dermal route. EPA plans to analyze dermal exposure for workers and ONUs to dust or mist that deposit on surfaces.

EPA is requesting information from the public about the following two occupational exposure scenarios that are among the scenarios that EPA plans to evaluate: dermal exposure of workers who handle articles containing D4 resulting from migration of D4 from these articles; and worker and ONU inhalation exposure at landfills to D4 vapor and dust containing D4.

Workers and ONUs may inadvertently ingest inhaled particles that deposit in the upper respiratory tract. In addition, workers may transfer chemicals from their hands to their mouths. The frequency and significance of this exposure route are dependent on several factors including the physical and chemical properties of the substance during worker activities, the visibility of the chemicals on the hands while working, workplace training and practices, and personal hygiene that is difficult to predict (Cherrie et al., 2006). EPA plans to consider the relevance of this exposure route on a case-by-case basis, taking into consideration the aforementioned factors and any reasonably available information, and may assess oral exposure for workers for certain COUs and worker activities where warranted. For certain conditions of use of D4, EPA plans to consider inhalation exposure to dust/particulates for workers and ONUs. As inhalation exposure to dust/particulates may occur, EPA plans to consider potential exposure for particulates that deposit in the upper respiratory tract from inhalation exposure and may be ingested via the oral route.

2.3.6 Consumer Exposures

Information contained in the submission requesting the risk evaluation for D4 along with CDR reporting and other sources indicate the presence of D4 in a number of consumer products and articles including: Adhesives and Sealants; Automotive Care Products; Furnishing, Cleaning, Treatment/Care Products; Paints and coatings; Plastic and rubber products not covered elsewhere (see Section 2.6.2 and Figure 2-14), (Docket ID: EPA-HQ-OPPT-2018-0443) (U.S. EPA, 2020a). These uses can result in exposures to consumers and bystanders (non-product users that are incidentally exposed to the product).

Based on reasonably available information on consumer conditions of use, inhalation of D4 is possible through either inhalation of vapor/mist during product usage or indoor air/dust. Oral exposure of D4 is possible through ingestion through product use via transfer from hand to mouth, through mouthing of articles, and through incidental ingestion of dust or vapor/mist containing D4. Dermal exposure may occur via contact with dust, vapor, or mist deposition onto the skin, via direct liquid contact during use, or direct dermal contact of articles containing D4. Based on these potential sources and pathways of exposure, EPA plans to analyze oral, dermal and inhalation exposures to consumers and inhalation

exposures to bystanders that may result from the conditions of use of D4 as described in Section 2.6.2 and the analysis plan.

2.3.7 General Population Exposures

Releases of D4 from certain conditions of use, such as manufacturing, processing, or disposal activities, may result in general population exposures. General population may be exposed via oral, dermal, or inhalation routes. The SEHSC submission (Docket ID: EPA-HQ-OPPT-2018-0443) considered the following pathways for general population for inhalation from ambient and indoor air, for ingestion via consumption of food items grown on soil containing D4, via drinking water, consumption of fish exposed to surface water or sediments containing D4, subsistence fishing and human milk, and for dermal absorption from use of products containing D4. The SEHSC submission exposure assessment of the general population was based on Gentry et al. (2017) and EC/HC (2008). In addition, preliminary information suggests that D4 may bioaccumulate in fish, EPA plans to review the information available for ingestion via consumption of fish and subsequent bioaccumulation to the general population. EPA plans to review the information contained in the SEHSC submission requesting the risk evaluation for D4 (Docket ID: EPA-HQ-OPPT-2018-0443) as well as other reasonably available information for the presence of D4 in environmental media relevant to general population exposure.

EPA identified studies reporting that D4 degrades into DMSD in water, soil, and sediment via different intermediate degradants under specific field and laboratory conditions (see Section 2.3.2). Concentrations of DMSD in soil, surface water, groundwater or drinking water could provide information for general population exposure to D4 degradants. Therefore, EPA is requesting information from the public on the concentration of DMSD and intermediate degradant products in these environmental media.

Human biomonitoring data exist, including three studies that collected and measured D4 concentrations in plasma. The 2019 SEHSC submission (Docket ID: EPA-HQ-OPPT-2018-0443) references the following biomonitoring studies. Xu et al. (2012) reported D4 plasma concentrations ranged from 4.56 to 57.8 ng/g for residents near a siloxane manufacturing facility. Hanssen et al. (2013) reported D4 plasma concentrations ranged from 12.7 to 20.93 ng/mL for postmenopausal women and 1.70 to 2.69 ng/mL for pregnant women. Fromme et al. (2015) reported a maximum D4 concentration in blood of 0.73 µg/L for adults (21 females and males of 20 to 68 years).

The presence in environmental media and biomonitoring data suggest that general population exposures are occurring. EPA plans to review reasonably available information related to general population exposures in the risk evaluation. The general population pathways in the scope of this evaluation are described in Section 2.6.3.

2.4 Hazards (Effects)

2.4.1 Environmental Hazards

EPA considered information in the SEHSC submission requesting the risk evaluation for D4 (Docket ID: EPA-HQ-OPPT-2018-0443) and all other reasonably available information (*e.g.*, federal and international government chemical assessments). Using automated techniques during the data screening phase of systematic review, EPA identified the following potential hazard effects for aquatic and terrestrial organisms, along with related information that may be considered for the risk evaluation (as explained in Appendix A): ADME, developmental, gastrointestinal, mortality, neurological, nutritional and metabolic, reproductive, and respiratory (Figure 2-10). A summary of references identified during the screening step of systematic review is included in the interactive literature inventory trees (Figure 2-9). As EPA continues to evaluate reasonably available and relevant hazard information identified through systematic review, EPA may update the list of potential hazard effects to be analyzed in the risk evaluation.

As described in Section 2.3.2, EPA identified studies reporting that D4 degrades into DMSD in water, soil, and sediment via different intermediate degradants under various conditions. Concentrations of DMSD in water, soil, and sediment could provide information for environmental exposure assessment to D4 degradants. Therefore, EPA is requesting information from the public on the toxicity of DMSD and the intermediate degradation products of D4.

2.4.2 Human Health Hazards

EPA considered information in the SEHSC submission requesting the risk evaluation for D4 (Docket ID: EPA-HQ-OPPT-2018-0443) and all other reasonably available information (*e.g.*, federal and international government chemical assessments). Using automated techniques during the data screening phase of systematic review, EPA identified the following potential human health hazards, along with related information that may be considered for the risk evaluation (as explained in Appendix A): ADME, cancer, endocrine, gastrointestinal, hematological and immune, hepatic, mortality, neurological, nutritional and metabolic, ocular and sensory, renal, reproductive, developmental, respiratory, skin and connective tissue (Figure 2-10). A summary of references identified during the screening step of systematic review is included in the interactive literature inventory trees (Figure 2-9). As EPA continues to evaluate reasonably available and relevant hazard information identified through systematic review, EPA may update the list of potential hazard effects to be analyzed in the risk evaluation.

As described in Section 2.3.2, EPA identified studies reporting that D4 degrades into DMSD in water, soil, and sediment via different intermediate degradants under various conditions. Concentrations of DMSD in water, soil, and sediment could provide information for the general population exposure assessment to D4 degradants. Therefore, EPA is requesting information from the public on the toxicity of DMSD and the intermediate degradation products of D4.

2.5 Potentially Exposed or Susceptible Subpopulations

TSCA section 6(b)(4) requires EPA to determine whether a chemical substance or category of chemical substances presents an unreasonable risk to "a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation." TSCA section 3(12) states that "the term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population for adverse health effects from exposure to a chemical substance or mixture, such as children, women who are or may become pregnant, workers, or the elderly." General population is "the total of individuals inhabiting an area or making up a whole group" and refers here to the U.S. general population (U.S. EPA, 2011a).

EPA plans to consider the following groups as PESS based on CDR information and studies reporting developmental and reproductive effects: children, women of reproductive age (*e.g.*, women who are or may become pregnant), workers, ONUs, consumers and bystanders, and indigenous, native populations as PESS in the risk evaluation. Other PESS may be identified based on reasonably available information.

EPA plans to increase consideration of environmental justice[6] issues by evaluating reasonably available evidence on factors that may make population groups of concern more vulnerable to adverse effects (*e.g.*, unique pathways; cumulative exposure from multiple stressors; and behavioral, biological, or environmental factors that increase susceptibility); identifying unique considerations for subsistence populations when relevant; and following best practices from EPA's *Technical Guidance for Assessing Environmental Justice in Regulatory Analysis* (U.S. EPA, 2016). EPA plans to include fenceline analyses where appropriate to screen for potential effects with emphasis on PESS and environmental justice communities, followed by more in-depth analysis where warranted. EPA will continue to develop the science of how to better consider different dimensions of susceptibility when selecting critical endpoints, PODs, determination of uncertainty factors and margins of exposure.

In developing exposure scenarios, EPA plans to analyze reasonably available information in order to determine whether some human receptor groups may be exposed via exposure pathways that may be distinct to a particular subpopulation or life stage (*e.g.*, reproductive age females who may be or become pregnant, lactating women, infants, toddlers, children at various developmental stages in life, and elderly) and whether some human receptor groups may have higher exposure via identified pathways of exposure due to unique characteristics (*e.g.*, activities, duration or location of exposure) when compared with the general population (U.S. EPA, 2006b). Likewise, EPA plans to evaluate reasonably available human health hazard information in order to determine whether some human receptor groups may have greater susceptibility than the general population to the chemical's hazard(s). Based on these analyses, EPA may expand the PESS considered in the risk evaluation.

[6] Additional information is available regarding EPA's Office of Environmental Justice.

2.6 Conceptual Models

In this section, EPA presents the conceptual models describing the identified exposures (pathways and routes), receptors, and hazards associated with the conditions of use of D4. Pathways and routes of exposure associated with workers and ONUs are described in Section 2.6.1, and pathways and routes of exposure associated with consumers are described in Section 2.6.2. Pathways and routes of exposure associated with environmental releases and wastes are discussed and depicted the conceptual model shown in Section 2.6.3.

2.6.1 Conceptual Model for Industrial and Commercial Activities and Uses

Figure 2-13 illustrates the conceptual model for the pathways of exposure from industrial and commercial activities and uses of D4 that EPA plans to include in the risk evaluation. There is potential for exposures to workers and/or occupational non-users via inhalation and dermal routes. Dermal exposure to D4 in both liquid and solid form is expected, as products and formulations containing D4 can be used/transported in liquid or solid form. EPA plans to evaluate activities resulting in exposures associated with distribution in commerce (*e.g.*, loading, unloading) throughout the various life cycle stages and conditions of use (*e.g.*, manufacturing, processing, industrial use, commercial use, and disposal) rather than a single distribution scenario.

Appendix F presents the combinations of exposure pathways, routes, and receptors for each condition of use identified in Table 2-2 along with supporting rationale for whether EPA plans to evaluate those combinations.

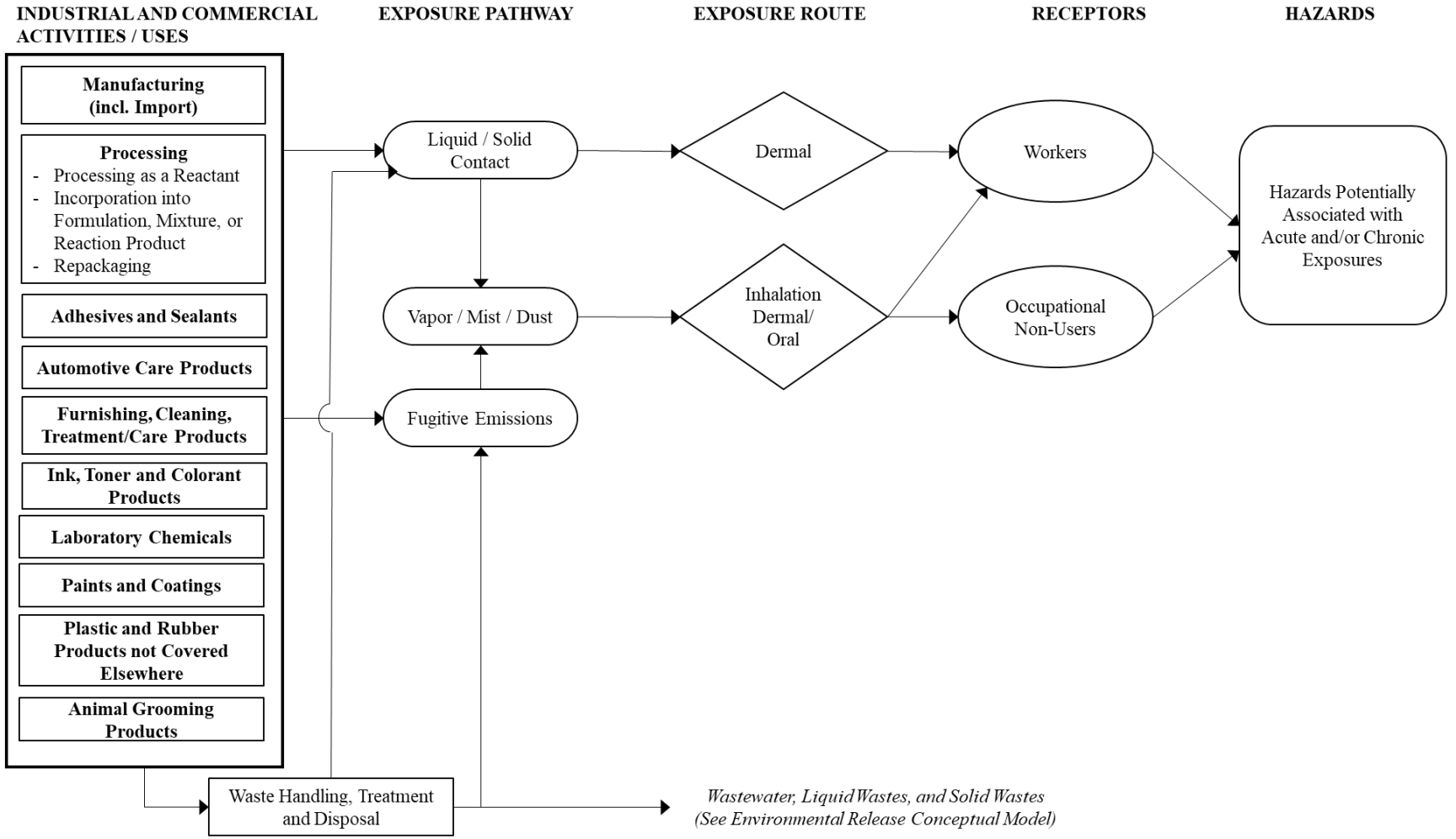

Figure 2-13. D4 Conceptual Model for Industrial and Commercial Activities and Uses: Worker and Occupational Non-user Exposures and Hazards[a]

The conceptual model presents the exposure pathways, exposure routes, and hazards to human receptors from industrial and commercial activities and uses of D4.

[a] Receptors include PESS (see Section 2.5)

2.6.2 Conceptual Model for Consumer Activities and Uses

The conceptual model in Figure 2-14 presents the exposure pathways, exposure routes, and hazards to human receptors from consumer activities and uses of D4. EPA expects that consumers and bystanders may be exposed through use of products or articles containing D4 via oral, dermal, and inhalation routes. An "article", as defined at 40 CFR 704.3, is distinct from a "product" in that an article is "a manufactured item:

1. which is formed to a specific shape or design during manufacture;
2. which has end use function(s) dependent in whole or in part upon its shape or design during end use; and
3. which has either no change of chemical composition during its end use or only those changes of composition which have no commercial purpose separate from that of the article, and that result from a chemical reaction that occurs upon end use of other chemical substances, mixtures, or articles; except that fluids and particles are not considered articles regardless of shape or design."

Additionally, during use of articles, EPA expects that consumers may also be exposed via direct dermal contact or mouthing (Figure 2-14). EPA plans to analyze pathways and routes of exposure that may occur during the varied identified consumer activities and uses. The supporting rationale for consumer pathways considered for D4 are included in Appendix G.

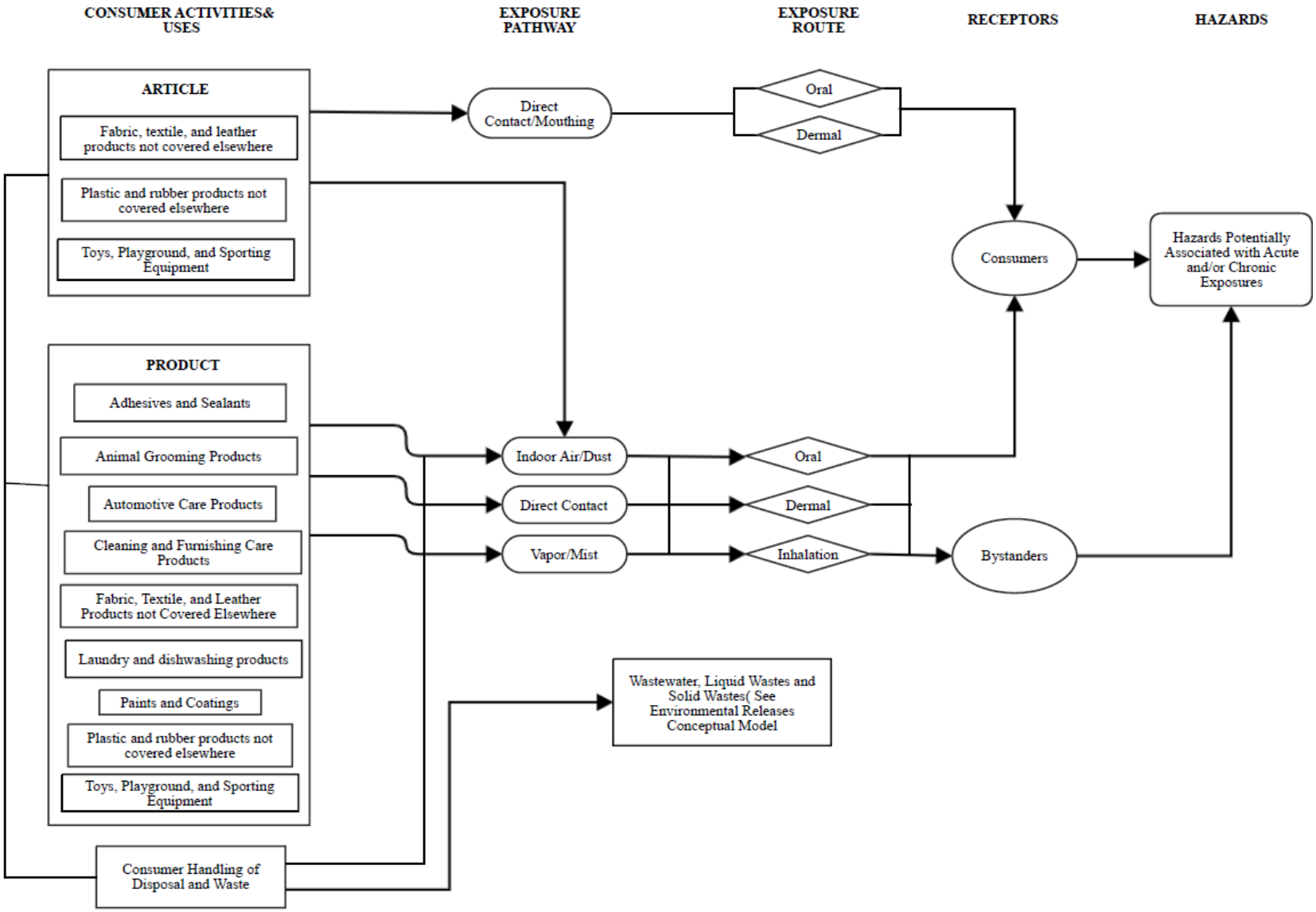

Figure 2-14. D4 Conceptual Model for Consumer Activities and Uses: Consumer Exposures and Hazards[a]

The conceptual model presents the exposure pathways, exposure routes, and hazards to human receptors from consumer activities and uses of D4.

[a] Receptors include PESS (see Section 2.5)

2.6.3 Conceptual Model for Environmental Releases and Wastes: Potential Exposures and Hazards

In this section, EPA presents the conceptual model describing the identified exposures (pathways and routes from environmental releases and wastes) and hazards to general population and environmental receptors associated with the conditions of use of D4 within the scope of the risk evaluation.

The conceptual model in Figure 2-15 presents the potential exposure pathways, exposure routes, and hazards to general population and environmental receptors from releases and waste streams associated with industrial, commercial, and consumer uses of D4 within the scope of the risk evaluation. EPA plans to evaluate exposures to receptors (*e.g.*, general population, aquatic and terrestrial species) that may occur from releases to air, releases to surface water, as well as indirect releases to drinking water and groundwater, and releases to land, including releases to landfill, biosolids and soil. EPA expects the general population to be exposed to D4 from air emissions via inhalation as well as from surface water, drinking water, liquid, and solid waste releases; orally via drinking water, fish and soil ingestion; and dermally from contact with groundwater, drinking water, and soil. The supporting rationale for general population and environmental pathways considered for D4 are included in Appendix H.

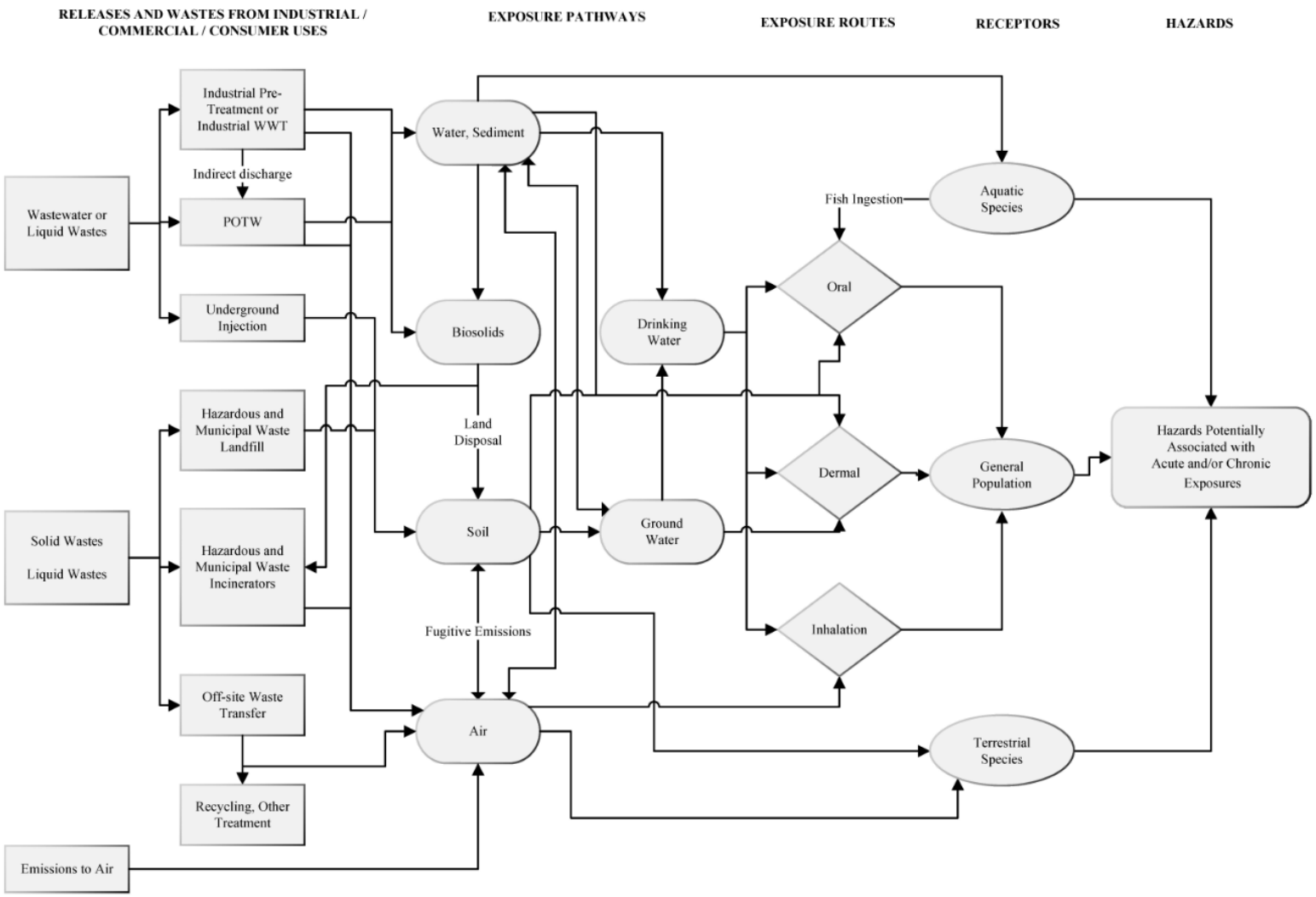

Figure 2-15. D4 Conceptual Model for Environmental Releases and Wastes: Environmental and General Population Exposures and Hazards

The conceptual model presents the exposure pathways, exposure routes, and hazards to human and environmental receptors from releases and wastes from industrial, commercial, and consumer uses of D4 that EPA plans to consider in the risk evaluation.

a. Industrial wastewater or liquid wastes may be treated on-site and then released to surface water (direct discharge), or pre-treated and released to publicly owned treatment works (POTW) (indirect discharge). For consumer uses, such wastes may be released directly to POTW. Drinking water will undergo further treatment in drinking water treatment plant. Groundwater may also be a source of drinking water. Inhalation from drinking water may occur via showering.

b. Receptors include PESS (see Section 2.5)

2.7 Analysis Plan

The analysis plan is based on EPA's knowledge of D4 resulting from the full-text screening of reasonably available information identified through EPA's literature searches as well as the information included in the SEHSC submission (see Section 2.1). EPA encourages submission of additional existing information, such as full study reports or workplace monitoring from industry sources, that may be relevant to EPA's evaluation of conditions of use, exposures, hazards, and PESS during the risk evaluation. Targeted supplemental searches during the analysis phase may be necessary to identify additional reasonably available information (*e.g.*, commercial mixtures) for the risk evaluation of D4. For any data needs identified during the risk evaluation, EPA may use the Agency's TSCA authorities under sections 4, 8, or 11, as appropriate.

2.7.1 Physical and Chemical Properties and Environmental Fate

EPA plans to analyze the physical and chemical properties and environmental fate and transport of D4 as follows:

1) **Review reasonably available measured or estimated physical and chemical properties and environmental fate endpoint data.**
   EPA plans to evaluate data and information submitted with the request for risk evaluation and collected through the systematic review process and public comments about the physical and chemical properties (Appendix B) and fate endpoints (Appendix C). EPA plans to evaluate all sources cited in EPA's analysis plan according to the procedures and metrics described in a draft systematic review protocol that EPA plans to release later this year. Where experimentally measured values for chemical properties are not reasonably available or of sufficiently high quality, values will be estimated using chemical parameter estimation models as appropriate. Model-estimated fate properties will be reviewed for applicability and quality.

2) **Using measured data and/or modeling, determine the influence of physical and chemical properties and environmental fate endpoints (*e.g.*, persistence, bioaccumulation, partitioning, transport) on exposure pathways and routes of exposure to human and environmental receptors.**
   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. The fate endpoints of interest include volatilization, sorption to organic matter in soil and sediments, water solubility, aqueous and atmospheric photolysis rates, aerobic and anaerobic biodegradation rates, and potential bioconcentration and bioaccumulation. EPA plans to use these endpoints in exposure calculations.

3) **Conduct a weight of the scientific evidence evaluation of physical and chemical properties and environmental fate data, including qualitative and quantitative sources of information.**
   During the risk evaluation, EPA plans to evaluate and integrate the physical and chemical property and environmental fate evidence identified in the literature inventory and in the SEHSC submission using revised systematic review methods described in a draft systematic review protocol that EPA plans to release later this year.

2.7.2 Exposure

EPA plans to analyze exposure levels for indoor dust, indoor air, ambient air, surface water, drinking water, groundwater, sediment, soil, biosolids, fish ingestion, aquatic biota, and terrestrial biota associated to exposure to D4. Based on their physical and chemical properties, expected sources, and

transport and transformation within the outdoor and indoor environment, D4 is more likely to be present in some of these media and less likely to be present in others. EPA has not yet determined the exposure levels in these media. Exposure level(s) can be characterized using a combination of reasonably available monitoring data and estimated exposure levels from modeling approaches. Exposure scenarios are combinations of sources (uses), exposure pathways, and exposed receptors. Draft exposure scenarios corresponding to various conditions of use for D4 are presented in Appendix F, Appendix G, and Appendix H. EPA plans to analyze scenario-specific exposures.

2.7.2.1 Environmental Releases

EPA plans to analyze releases to environmental media as follows:

1) **Review reasonably available published literature and other reasonably available information on processes and activities associated with the conditions of use to analyze the types of releases and wastes generated.**
   EPA has reviewed some sources containing information on processes and activities resulting in releases, and the information found is described in Appendix E. EPA plans to review additional data sources identified. Potential sources of environmental release data are summarized in Table 2-4 below:

   Table 2-4. Categories and Sources of Environmental Release Data

EPA Generic Scenarios
OECD Emission Scenario Documents
Environment Canada Screening Assessment for the Challenge, Octamethylcyclotetrasiloxane (D4), 2008
SEHSC D4 Environmental Testing Study Plan, Enforceable Consent Agreement, 2016, (Docket No. EPA-HQ-OPPT-2012-0209)
SEHSC submission (Docket No. EPA-HQ-OPPT-2018-0443-0004)

2) **Review reasonably available chemical-specific release data, including measured or estimated release data (*e.g.*, data from risk assessments by other environmental agencies).**
   EPA plans to evaluate additional reasonably available information during development of the risk evaluation. EPA plans to match identified data to applicable conditions of use and identify conditions of use for which data are limited. EPA plans to augment and/or supplement data through the use of models and potential surrogate data where appropriate.

   Additionally, for conditions of use where no measured data on releases are reasonably available, 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).

3) **Review reasonably available measured or estimated release data for surrogate chemicals that have similar uses and physical properties.**
   EPA plans to review literature sources identified, and if surrogate data are found, these data will be matched to applicable conditions of use to potentially augment and/or supplement existing data. Measured or estimated release data for other siloxanes may be considered as surrogates for D4.

4) **Review reasonably available data that may be used in developing, adapting, or applying exposure models to the particular risk evaluation.**
This item will be performed after completion of #2 and #3 above. EPA plans to evaluate relevant data to determine whether the data can be used to develop, adapt, or apply models for specific conditions of use (and corresponding release scenarios). EPA has identified information from various EPA statutes and sources (including, for example, regulatory limits, reporting thresholds or disposal requirements) that may be relevant to release estimation and environmental exposures. EPA plans to consider relevant regulatory requirements in estimating releases during risk evaluation.

5) **Review and determine applicability of OECD Emission Scenario Documents (ESDs) and EPA Generic Scenarios (GSs) to estimation of environmental releases.**
EPA has identified potentially relevant OECD Emission Scenario Documents (ESDs) and EPA Generic Scenarios (GSs) that correspond to some conditions of use; for example, the 2015 ESD on Use of Adhesives (OECD, 2015), the 2009 ESD on Adhesive Formulation (OECD, 2009a), the 2004 ESD on Rubber Additives (OECD, 2004), and the 2011 ESD on Radiation Curable Coating, Inks and Adhesives (OECD, 2011) may be useful to assess potential releases. EPA plans to critically review these ESDs and GSs to determine their applicability to the conditions of use assessed.

   If ESDs and GSs are not available, other methods may be considered. EPA may also perform supplemental targeted searches of peer-reviewed or gray literature for applicable models and associated parameters that EPA may use to estimate releases for certain conditions of use. Additionally, for conditions of use where no measured data on releases are reasonably available, EPA may use a variety of methods including the application of default assumptions such as standard loss fractions associated with drum cleaning (3%) or single process vessel cleanout (1%).

6) **Map or group each condition of use to a release assessment scenario(s).**
EPA has completed initial mapping of release scenarios to relevant conditions of use as shown in Appendix F. EPA plans to refine the mapping/grouping of release scenarios based on factors (*e.g.*, process equipment and handling, magnitude of production volume used, and exposure/release sources) corresponding to conditions of use using reasonably available information. EPA may perform supplemental targeted searches of peer-reviewed or gray literature to better understand certain conditions of use to further develop these release scenarios.

7) **Evaluate the weight of the scientific evidence of environmental release data.**
During risk evaluation, EPA plans to evaluate and integrate the environmental release evidence identified in the literature inventory using revised systematic review methods described in a draft systematic review protocol that EPA plans to release later this year. EPA plans to integrate the data using systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

2.7.2.2 Environmental Exposures

EPA plans to analyze the following in developing its environmental exposure assessment of D4:

1) **Review reasonably available environmental and biological monitoring data for all media relevant to environmental exposure.**
   For D4, environmental media which EPA plans to analyze are sediment, soil, biosolids, air, drinking water, groundwater, and surface water.

2) **Review reasonably available information on releases to determine how modeled estimates of concentrations near industrial point sources compare with reasonably available monitoring data.**
   EPA plans to analyze and consider reasonably available environmental exposure models that meet the scientific standards under TSCA section 26(h) and that estimate air, surface water, groundwater, sediment, biosolids, and soil concentrations alongside reasonably available air, surface water, groundwater, sediment, and soil monitoring data to characterize environmental exposures. Modeling approaches to estimate air concentrations, surface water concentrations, sediment concentrations, biosolids concentrations, and soil concentrations may generally include the following inputs: direct release into air, groundwater, surface water, sediment, or soil, indirect release into air, groundwater, surface water, sediment, or soil *(i.e.*, air deposition), fate and transport (partitioning within media) and characteristics of the environment (*e.g.*, river flow, volume of lake, meteorological data).

3) **Determine applicability of existing additional contextualizing information for any monitored data or modeled estimates during risk evaluation.**
   EPA plans to evaluate any studies which relate levels of D4 in the environment or biota with specific sources or groups of sources. EPA plans to review and characterize monitoring data or modeled estimates to determine how representative they are of ongoing use patterns.

4) **Group each condition(s) of use to environmental assessment scenario(s).**
   EPA plans to refine and finalize exposure scenarios for environmental receptors by considering combinations of sources (use descriptors), exposure pathways including routes, and populations exposed. For D4, the following are noteworthy considerations in constructing exposure scenarios for environmental receptors:
   - Estimates of air concentrations, groundwater concentrations, surface water concentrations, sediment concentrations and soil concentrations near industrial point sources based on reasonably available monitoring data;
   - Consider the following modeling inputs: release into the media of interest, fate and transport and characteristics of the environment;
   - Reasonably available biomonitoring data. Monitoring data could be used to compare with species or taxa-specific toxicological benchmarks;
   - Applicability of existing additional contextualizing information for any monitored data or modeled estimates during risk evaluation. Review and characterize the spatial and temporal variability, to the extent that data are reasonably available, and characterize exposed aquatic and terrestrial populations; and
   - Weight of the scientific evidence of environmental occurrence data and modeled estimates.

5) **Evaluate the weight of the scientific evidence of environmental occurrence data and modeled estimates.**
During risk evaluation, EPA plans to evaluate and integrate the exposure evidence identified in the literature inventory using revised systematic review methods described in a draft systematic review protocol that EPA plans to release later this year.

2.7.2.3 Occupational Exposures

EPA plans to analyze both worker and occupational non-user exposures as follows:

1) **Review reasonably available exposure monitoring data for specific condition(s) of use.**
EPA plans to review exposure data including workplace monitoring data collected by government agencies such as OSHA and NIOSH, as well as monitoring data found in published literature, and any relevant information provided in the SEHSC submission. These workplace monitoring data include personal exposure monitoring data (direct exposures) and area monitoring data (indirect exposures).

   EPA has also identified additional data sources that may contain relevant monitoring data for the various conditions of use. EPA plans to review these sources (identified in Table 2-5) and extract relevant data for consideration and analysis during risk evaluation.

Table 2-5. Potential Sources of Occupational Exposure Data

Environment Canada Screening Assessment for the Challenge, Octamethylcyclotetrasiloxane (D4), 2008
Gentry at al., 2017. *A Global Human Health Risk Assessment for Octamethylcyclotetrasiloxane (D4)*.
EPA-HQ-OPPT-2018-0443-0004

2) **Review reasonably available exposure data for surrogate chemicals that have uses, volatility and physical and chemical properties similar to D4.**
EPA plans to review literature sources submitted in the SEHSC submission and identified through systematic review, and if surrogate data are found, these data will be matched to applicable conditions of use for potentially filling data gaps.

3) **For conditions of use where data are limited or not reasonably available, review existing exposure models that may be applicable in estimating exposure levels.**
EPA has identified potentially relevant OECD Emission Scenario Documents (ESDs) and EPA Generic Scenarios (GSs) corresponding to some conditions of use. For example, the 2015 ESD on the Use of Adhesives (OECD, 2015) and the 2011 ESD on Radiation Curable Coating, Inks and Adhesives (OECD, 2011) are some of the ESDs and GSs that EPA may use to estimate occupational exposures. EPA plans to critically review these ESDs and GSs to determine their applicability to the conditions of use assessed. EPA may conduct or perform supplemental targeted searches of peer-reviewed or gray literature to understand those conditions of use, which may inform identification of exposure scenarios. EPA may also need to perform targeted supplemental searches to identify applicable models that EPA may use to estimate exposures for certain conditions of use.

4) **Review reasonably available data that may be used in developing, adapting, or applying exposure models to a particular risk evaluation scenario.**
This step will be performed after #2 and #3 are completed. Based on information developed from #2 and #3, EPA plans to evaluate relevant data to determine whether the data can be used to develop, adapt, or apply models for specific conditions of use (and corresponding exposure scenarios). EPA may utilize existing, peer-reviewed exposure models developed by EPA, other government agencies, or reasonably available in the scientific literature, or EPA may elect to develop additional models to assess specific condition(s) of use. Inhalation exposure models may be simple box models or two-zone (near-field/far-field) models. In two-zone models, the near-field exposure represents potential inhalation exposures to workers, and the far-field exposure represents potential inhalation exposures to ONUs.

5) **Consider and incorporate applicable engineering controls and/or PPE into exposure scenarios.**
In the risk evaluation, EPA plans to examine the effects of engineering controls and PPE on occupational exposures to support any potential risk management in the event of an unreasonable risk determination. 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.*, respirator).

6) **Map or group each condition of use to occupational exposure assessment scenario(s).** EPA has identified occupational exposure scenarios and mapped them to relevant conditions of use (see Appendix F). As presented in the fourth column in Table_Apx F-1, EPA has completed an initial mapping of exposure scenarios to conditions of use. 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 plans to consider information submitted through public comment and may perform supplemental targeted searches of peer-reviewed or gray literature to better understand certain conditions of use to further develop exposure scenarios.

7) **Evaluate the weight of the scientific evidence of occupational exposure data, which may include qualitative and quantitative sources of information.**
During risk evaluation, EPA plans to evaluate and integrate the exposure evidence identified in the literature inventory using revised systematic review methods described in a draft systematic review protocol that EPA plans to release later this year. EPA plans to rely on the weight of the scientific evidence when evaluating and integrating occupational data. EPA plans to integrate the data using systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

2.7.2.4 Consumer Exposures

EPA plans to analyze both consumers using a consumer product and bystanders associated with the consumer using the product as follows:

1) **Group each condition of use to consumer exposure assessment scenario(s).**
   EPA plans to refine and finalize exposure scenarios for consumers by considering combinations of sources (ongoing consumer uses), exposure pathways including routes, and exposed populations.

   For D4, the following are noteworthy considerations in constructing consumer exposure scenarios:

   - Conditions of use and type of consumer product;
   - Duration, frequency, and magnitude of exposure;
   - Weight fraction of chemical in products; and
   - Amount of chemical used.

2) **Evaluate the relative potential of indoor exposure pathways based on reasonably available data.**
   Indoor exposures may include dust ingestion, mouthing of products, inhalation of indoor air and dust, and dermal contact with dust, articles, and product use. EPA plans to evaluate all reasonably available information in developing the consumer exposure scenarios and evaluating the exposure pathways in indoor environments.

3) **Review existing indoor exposure models that may be applicable in estimating indoor air concentrations.**
   Indoor exposure models that estimate emissions from consumer products are available. These models generally consider physical and chemical properties (*e.g.*, vapor pressure, molecular weight), product specific properties (*e.g.*, weight fraction of the chemical in the product), use patterns (*e.g.*, duration and frequency of use), user environment (*e.g.*, room of use, ventilation rates), and receptor characteristics (*e.g.*, exposure factors, activity patterns). The OPPT's Consumer Exposure Model (CEM) and other similar models can be used to estimate indoor air exposures from consumer products.

   Indoor exposure models that estimate emission and migration of SVOCs into the indoor environment are available. These models generally consider mass transfer as informed by the gas-phase mass transfer coefficient, the solid-phase diffusion coefficient, and the material-air partition coefficient. These properties vary based on physical and chemical properties and properties of the material. The OPPT's Indoor Environmental Concentrations in Buildings with Conditioned and Unconditioned Zones (IECCU) model and other similar models can be used to estimate indoor air and dust exposures from indoor sources.

4) **Review reasonably available empirical data that may be used in developing, adapting, or applying exposure models to a particular risk evaluation scenario. For example, existing models developed for a chemical assessment may be applicable to another chemical assessment if model parameter data are reasonably available.**
   To the extent other organizations have already modeled a D4 consumer exposure scenario that is relevant to the OPPT's assessment (*e.g.*, Gentry et al., 2017, EC/HC, 2008), EPA plans to evaluate those modeled estimates as well as modeled estimates for any other chemicals similar to

D4 that have been modeled for similar uses. The underlying parameters and assumptions of the models will also be evaluated.

5) **Review reasonably available consumer product-specific sources to determine how those exposure estimates compare with each other and with indoor monitoring data reporting D4 in specific media (*e.g.*, indoor air).**
EPA plans to evaluate the availability of D4 concentration for various ongoing uses. These data provide the source term for any subsequent indoor modeling. EPA plans to analyze source attribution between overall indoor air levels and various indoor sources.

6) **Review reasonably available population- or subpopulation-specific exposure factors and activity patterns to determine if PESS need to be further refined.**
For D4, EPA plans to evaluate exposure scenarios that involve PESS and plans to consider age-specific behaviors, activity patterns and exposure factors unique to those subpopulations. For some exposure scenarios related to consumer uses, EPA plans to consider whether exposures for adults may differ from those of children due to different activities (*e.g.*, children may mouth certain products) or exposure factors (*e.g.*, inhalation rates).

7) **Evaluate the weight of the scientific evidence of consumer exposure estimates based on different approaches.**
EPA plans to rely on the weight of the scientific evidence when evaluating and integrating data related to consumer exposure. The weight of the scientific evidence may include qualitative and quantitative sources of information. EPA plans to integrate the data using systematic review methods to assemble the relevant data, evaluate the data for quality and relevance, including strengths and limitations, followed by synthesis and integration of the evidence.

2.7.2.5 General Population

EPA plans to analyze general population exposures as follows:

1) **Refine and finalize exposure scenarios for general population by considering combinations of sources and uses, exposure pathways including routes, and exposed populations.**
For D4, the following are noteworthy considerations in constructing exposure scenarios for the general population:

- Review reasonably available environmental and biological monitoring data for media to which general population exposures are expected;
- For exposure pathways where data are not reasonably available, review existing exposure models that may be applicable in estimating exposure levels;
- Consider and incorporate applicable media-specific regulations into exposure scenarios or modeling;
- Review reasonably available data that may be used in developing, adapting, or applying exposure models to the particular risk evaluation. For example, existing models developed for a chemical assessment may be applicable to another chemical assessment if model parameter data are reasonably available;
- Review reasonably available information on releases to determine how modeled estimates of concentrations near industrial point sources compare with reasonably available monitoring data;
- Review reasonably available population- or subpopulation-specific exposure factors and activity patterns to determine if PESS need to be further defined;

- Develop approaches and methodologies that use reasonably available information, modeling, and geospatial analysis to evaluate impacts to population groups of concern (*e.g.*, fenceline and environmental justice communities);
- Evaluate the weight of the scientific evidence of general population exposure data; and
- Map or group each condition of use to general population exposure assessment scenario(s).

EPA plans to evaluate a variety of data types to determine which types are most appropriate when quantifying exposure scenarios. Environmental monitoring data, biomonitoring data, modeled estimates, experimental data, epidemiological data, and survey-based data can all be used to quantify exposure scenarios. EPA anticipates that there will be a range in the potential exposures associated with the exposure scenarios identified in Section 2.6.

After refining and finalizing exposure scenarios, EPA plans to quantify concentrations and/or doses for these scenarios. The number of scenarios will depend on how combinations of uses, exposure pathways, and receptors are characterized. The number of scenarios is also dependent upon the reasonably available data and approaches to quantify scenarios. When quantifying exposure scenarios, EPA plans to use a tiered approach. First-tier analysis is based on data that is reasonably available without a significant number of additional inputs or assumptions, and may be qualitative, semi-quantitative, or quantitative. The results of first tier analyses inform whether scenarios require more refined analysis. Refined analyses will be iterative and require careful consideration of variability and uncertainty.

2) **For exposure pathways where empirical data are not reasonably available, review existing exposure models that may be applicable in estimating exposure levels.**
For D4, media where exposure models may be considered for general population exposure include models that estimate ambient air concentrations, drinking water concentrations, surface water concentrations, groundwater concentrations, sediment concentrations, soil concentrations, and uptake from aquatic and terrestrial environments into edible aquatic and terrestrial organisms.

3) **Review reasonably available exposure modeled estimates. For example, existing models developed for a previous D4 chemical assessment may be applicable to EPA's assessment. In addition, another chemical's assessment may also be applicable if model parameter data are reasonably available.**
To the extent other organizations have already modeled D4 general population exposure scenario that is relevant to this assessment, EPA plans to evaluate those modeled estimates. In addition, if modeled estimates for other chemicals with similar physical and chemical properties and similar uses are reasonably available, EPA plans to evaluate those modeled estimates, along with their underlying parameters and assumptions.

4) **Review reasonably available information on releases to determine how modeled estimates of concentrations near industrial point sources compare with reasonably available monitoring data.**
The expected releases from industrial facilities are changing over time. EPA plans to carefully compare any modeled concentrations based on recent release estimates with reasonably available monitoring data to determine representativeness.

5) **Review reasonably available information about population- or subpopulation-specific exposure factors and activity patterns to determine if PESS need to be further defined (*e.g.*, early life and/or puberty as a potential critical window of exposure).**
EPA plans to consider age-specific behaviors, activity patterns, and exposure factors unique to any PESS for exposure scenarios that involve those subpopulations (*e.g.*, children may have different intake rates for soil than adults; infants may be exposed via ingestion of human milk).

6) **Evaluate the weight of the scientific evidence of general population exposure estimates based on different approaches.**
During risk evaluation, EPA plans to evaluate and integrate the exposure evidence submitted in the request for risk evaluation as well as evidence identified in the literature inventory using revised systematic review methods described in a draft systematic review protocol that EPA plans to release later this year.

2.7.3 Hazards (Effects)

2.7.3.1 Environmental Hazards

EPA plans to conduct an environmental hazard assessment of D4 as follows:

1) **Review reasonably available environmental hazard data, including data from alternative test methods (*e.g.*, computational toxicology and bioinformatics; high-throughput screening methods; data on categories and read-across; in vitro studies).**
EPA plans to analyze the hazards of D4 to aquatic and/or terrestrial organisms, including plants, invertebrates (*e.g.*, insects, arachnids, mollusks, crustaceans), and vertebrates (*e.g.*, mammals, birds, amphibians, fish, reptiles) across exposure durations and conditions if potential environmental hazards are identified through the SEHSC submission, systematic review results, or public comments. EPA also plans to consider additional types of environmental hazard information (*e.g.*, analogue and read-across data) when characterizing the potential hazards of D4 to aquatic and/or terrestrial organisms.

   EPA plans to evaluate environmental hazard data using revised evaluation strategies described in a draft systematic review protocol that EPA plans to release later this year. The study evaluation results will be documented in the risk evaluation phase and data from acceptable studies will be extracted and integrated in the risk evaluation process.

   Mechanistic data may include analyses of alternative test data such as novel *in vitro* test methods and high throughput screening, which will be integrated in the risk evaluation process for hazard and risk characterization *(i.e.*, determination of MOA key events, susceptibility factors, human relevance). The association between acute and chronic exposure scenarios to the agent and each health outcome will also be integrated. Study results will be extracted and presented in evidence tables or another appropriate format by organ/system.

2) **Derive hazard thresholds for aquatic and/or terrestrial organisms.**
Depending on the robustness of the evaluated data for a particular organism or taxa (*e.g.*, aquatic invertebrates), environmental hazard values (*e.g.*, EC_x, LC_x, NOEC, LOEC) may be derived and used to further understand the hazard characteristics of D4 to aquatic and/or terrestrial species. Identified environmental hazard thresholds may be used to derive concentrations of concern (COC), based on endpoints that may affect populations of organisms or taxa analyzed.

3) **Evaluate the weight of the scientific evidence of environmental hazard data.**
During risk evaluation, EPA plans to evaluate and integrate the environmental hazard evidence identified in the literature inventory using revised systematic review methods described in a draft systematic review protocol that EPA plans to release later this year.

4) **Consider the route(s) of exposure, based on reasonably available monitoring and modeling data and other reasonably available approaches to integrate exposure and hazard assessments.**
EPA plans to consider aquatic (*e.g.*, water and sediment exposures) and terrestrial pathways in the D4 conceptual model (Figure 2-15). These organisms may be exposed to D4 via a number of environmental pathways (*e.g.*, air, surface water, sediment, soil, diet).

5) **Consider a persistent, bioaccumulative, and toxic (PBT) assessment of D4.**
EPA plans to consider the persistence, bioaccumulation, and toxic (PBT) potential of D4 after reviewing relevant physical and chemical properties and exposure pathways. EPA plans to assess the studies submitted in the request for risk evaluation as well as reasonably available studies collected from the systematic review process relating to bioaccumulation and bioconcentration (*e.g.*, BAF, BCF) of D4. In addition, EPA plans to integrate traditional environmental hazard endpoint values (*e.g.*, LC_{50}, LOEC) and exposure concentrations (*e.g.*, surface water concentrations, tissue concentrations) for D4 with the fate parameters (*e.g.*, BAF, BCF, BMF, TMF).

2.7.3.2 Human Health Hazards

EPA plans to analyze human health hazards as follows:

1) **Review reasonably available human health hazard data, including data from human and animal studies (human health animal models defined in Table_Apx A-4) and alternative test methods (*e.g.*, computational toxicology and bioinformatics; high-throughput screening methods; data on categories and read-across; *in vitro* studies; systems biology).**
EPA plans to evaluate human health studies using revised evaluation strategies described in a draft systematic review protocol that EPA plans to release later this year. These evaluation strategies also apply to human health studies described in the SEHSC submission for D4 (EPA-HQ-OPPT-2018-0443). EPA plans to document the study evaluation results in the risk evaluation phase; to extract data from acceptable studies; and to integrate those data into the risk evaluation process.

   Mechanistic data may include analyses of alternative test data such as novel *in vitro* test methods and high throughput screening, which will be integrated in the risk evaluation process for hazard and risk characterization *(i.e.*, determination of MOA key events, susceptibility factors, human relevance). The association between acute and chronic exposure scenarios to the agent and each health outcome will also be integrated. Study results will be extracted and presented in evidence tables or another appropriate format by organ/system.

2) **In evaluating reasonably available data, identify any PESS that may have greater susceptibility to the chemical's hazard(s) than the general population.**
Reasonably available human health hazard data will be evaluated to ascertain whether some human receptor groups may have greater susceptibility than the general population to D4 hazard(s). Susceptibility of particular human receptor groups to D4 will be determined by evaluating information on factors that influence susceptibility.

EPA has reviewed some sources containing hazard information associated with PESS and lifestages such as pregnant women and infants. Women of childbearing age (and those who may become pregnant) were identified as a sensitive subpopulation. Pregnancy (*i.e.*, gestation) and childhood are potential susceptible lifestages for D4 exposure. EPA may quantify these differences in the risk evaluation following further evaluation of the reasonably available data and information. If the reasonably available data and information are insufficient for the identification of human health hazard endpoints for PESS, EPA will consider alternative approaches including consideration of the identified susceptibility factors in the application of an intraspecies uncertainty/variability factor in the risk characterization.

3) **Conduct hazard identification (the qualitative process of identifying non-cancer and cancer endpoints) and dose-response assessment (the quantitative relationship between hazard and exposure) for identified human health hazard endpoints.**
Human health hazards from acute and chronic exposures will be identified by evaluating the human and animal data that meet the revised systematic review data quality criteria, which will be described in a draft systematic review protocol that EPA plans to release later this year. Hazards identified by studies meeting acceptable data quality criteria will be grouped by routes of exposure relevant to humans (*e.g.*, oral, dermal, inhalation) and by cancer and non-cancer endpoints identified in Section 2.4.2.

   Dose-response assessment will be performed in accordance with EPA guidance (U.S. EPA, 2012a, 2011b, 1994) developing points of departure (POD) for either margins of exposure (MOEs), cancer slope factors (CSFs), oral slope factors (OSFs), and/or inhalation unit risks (IURs). Dose-response analyses may be used if the data meet data quality criteria and if additional information on the identified hazard endpoints are not reasonably available or would not alter the analysis.

   The cancer mode of action (MOA) analyses determine the relevancy of animal data to human risk and how data can be quantitatively evaluated. If the D4 cancer hazard is determined to be relevant to humans, EPA plans to evaluate information on genotoxicity and the MOA for all cancer endpoints to determine the appropriate approach for quantitative cancer assessment in accordance with the *U.S. EPA Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005a). In accordance with EPA's *Supplemental Guidance for Assessing Susceptibility from Early-life Exposures to Carcinogens* (U.S. EPA, 2005b), EPA plans to determine whether age-dependent adjustment factors (ADAFs) are appropriate for D4 for specific conditions of use based upon potential exposures to children.

4) **Derive points of departure (PODs) where appropriate; conduct benchmark dose modeling depending on the reasonably available data. Adjust the PODs as appropriate to conform (*e.g.*, adjust for duration of exposure) to the specific exposure scenarios evaluated.**
EPA plans to evaluate hazard data to determine the type of dose-response modeling that is applicable. Where modeling is feasible, a set of dose-response models that are consistent with a variety of potentially underlying biological processes will be applied to empirically model the dose-response relationships in the range of the observed data consistent with EPA's *Benchmark Dose Technical Guidance Document* (U.S. EPA, 2012a). Where dose-response modeling is not feasible, no observed adverse effect levels (NOAELs) or lowest observed adverse effect levels (LOAELs) will be identified. Non-quantitative data will also be evaluated for contribution to the weight of the scientific evidence or for evaluation of qualitative endpoints that are not appropriate for dose-response assessment.

EPA plans to evaluate whether the reasonably available PBPK and empirical kinetic models are adequate for route-to-route and interspecies extrapolation of the POD, or for extrapolation of the POD to standard exposure durations (*e.g.*, lifetime continuous exposure). If application of the PBPK model is not possible, oral PODs may be adjusted by $BW^{3/4}$ scaling in accordance with U.S. EPA (2011b), and inhalation PODs may be adjusted by exposure duration and chemical properties in accordance with (U.S. EPA, 1994).

5) **Evaluate the weight of the scientific evidence of human health hazard data.**
During risk evaluation, EPA plans to evaluate and integrate the human health hazard evidence identified in the literature inventory under acute and chronic exposure conditions using revised systematic review methods described in a draft systematic review protocol that EPA plans to release later this year.

6) **Consider the route(s) of exposure (*e.g.*, oral, inhalation, dermal), reasonably available route-to-route extrapolation approaches; biomonitoring data; and approaches to correlate internal and external exposures to integrate exposure and hazard assessment.**
EPA plans to evaluate the reasonably available data to determine whether it is sufficient to conduct dose-response analysis and/or benchmark dose modeling for the oral route of exposure. EPA plans to also evaluate any potential human health hazards following dermal and inhalation exposure to D4, which could be important for worker, consumer, and general population risk analysis. Reasonably available data will be assessed to determine whether or not a point of departure can be identified for the dermal and inhalation routes.

   If sufficient reasonably available toxicity studies are not identified through the systematic review process to assess risks from dermal or inhalation exposures, then a route-to-route extrapolation from oral toxicity studies may be needed. The preferred approach is to use a PBPK model (U.S. EPA, 2006a). Without an adequate PBPK model, considerations regarding the adequacy of data for route-to-route extrapolation are described in *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (U.S. EPA, 1994). EPA may use these considerations when determining whether to extrapolate from the oral to the inhalation route of exposure. Similar approaches for oral-to-dermal route extrapolation are described in EPA guidance document *Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment)* (U.S. EPA, 2004).

   If there are acceptable oral and inhalation data after completion of systematic review, EPA may also consider extrapolating from the inhalation to the dermal route if first-pass metabolism through the liver via the oral route is expected because in that case, use of data from the oral route is not recommended (U.S. EPA, 1994). EPA may also consider inhalation-to-dermal route extrapolation if an inhalation toxicity study with a sensitive hazard endpoint is used to evaluate risks. Based on these considerations, EPA extrapolated from the inhalation to the dermal route for the methylene chloride (U.S. EPA, 2020d), carbon tetrachloride (U.S. EPA, 2020b) and perchloroethylene (U.S. EPA, 2020c) risk evaluations under amended TSCA.

2.7.4 Summary of Risk Approaches for Characterization

EPA plans to conduct a risk estimation and characterization of D4 to identify if there are risks to the environment or human health. For environmental risk characterization, EPA plans to identify if there are risks to aquatic and/or terrestrial environments from the measured and/or predicted concentrations of D4 in environmental media (*e.g.*, air, water, sediment, soil). Risk quotients (RQs) may be derived by the

application of hazard and exposure benchmarks to characterize environmental risk (U.S. EPA, 1998; Barnthouse et al., 1982). Similarly, for human health risk characterization, EPA plans to integrate exposure estimates from measured and/or modeled data with hazard data to characterize risk to human health. Analysis of environmental or human health risk for characterization includes a confidence statement in risk estimation. This confidence statement is based on qualitative judgment describing the certainty of the risk estimate considering the strength of the evidence scores for hazard and exposure along with their limitations and relevance. The lowest confidence evaluation for either hazard or exposure will drive the overall confidence estimate.

Risk characterization is an integral component of the risk assessment process for both environmental and human health risks. EPA plans to derive the risk characterization in accordance with EPA's *Risk Characterization Handbook* (U.S. EPA, 2000). As defined in EPA's Risk Characterization Policy, "the risk characterization integrates information from the preceding components of the risk evaluation and synthesizes an overall conclusion about risk that is complete, informative and useful for decision makers." Risk characterization is considered to be a conscious and deliberate process to bring all important considerations about risk, not only the likelihood of the risk but also the strengths and limitations of the assessment, and a description of how others have assessed the risk into an integrated picture.

The level of information contained in each risk characterization varies according to the type of assessment for which the characterization is written. Regardless of the level of complexity or information, the risk characterization for TSCA risk evaluations 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). As discussed in 40 CFR 702.43, risk characterization has a number of considerations. This is the step where EPA integrates the hazard and exposure assessments into risk estimates for the identified populations (including any PESS) and ecological characteristics and weighs the scientific evidence for the identified hazards and exposures. The risk characterization does not consider costs or other non-risk factors, and takes into account, "where relevant, the likely duration, intensity, frequency, and number of exposures under the condition(s) of use…." The risk characterization also summarizes the following considerations: (1) uncertainty and variability in each step of the risk evaluation; (2) data quality, and any applicable assumptions used; (3) alternative interpretations of data and analyses, where appropriate; and (4) any considerations for environmental risk evaluations, if necessary (*e.g.*, related to nature and magnitude of effects).

EPA also plans to be guided by EPA's Information Quality Guidelines (U.S. EPA, 2002) as it provides guidance for presenting risk information. Consistent with those guidelines, EPA plans to identify in the risk characterization the following: (1) each population addressed by an estimate of applicable risk effects; (2) the expected risk or central estimate of risk for the PESS affected; (3) each appropriate upper-bound or lower-bound estimate of risk; (4) each significant uncertainty identified in the process of the assessment of risk effects and the studies that would assist in resolving the uncertainty; and (5) peer-reviewed studies known to the Agency that support, are directly relevant to, or fail to support any estimate of risk effects and the methodology used to reconcile inconsistencies in the scientific information.

2.8 Peer Review

The draft risk evaluation for D4 will be peer reviewed. Peer review will be conducted in accordance with EPA's regulatory procedures for chemical risk evaluations, including using EPA's *Peer Review Handbook* (U.S. EPA, 2015b) and other methods consistent with section 26 of TSCA (see 40 CFR 702.45). As explained in the final rule *Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act* (82 FR 33726, 33744; July 20, 2017), the purpose of peer review is for the independent review of the science underlying the risk assessment. Peer review will therefore address aspects of the underlying science as outlined in the charge to the peer review panel such as hazard assessment, assessment of dose-response, exposure assessment, and risk characterization.

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APPENDICES

Appendix A ABBREVIATED METHODS FOR SEARCHING AND SCREENING

A.1 Literature Search of Publicly Available Databases

A.1.1 Search Term Genesis and Chemical Verification

To develop the chemical terms for the subsequent literature search for D4, several online sources were queried.

- ChemSpider (Royal Society of Chemistry)
- ChemIDplus (NLM)
- FDA Substance Registration System
- ECHA (European Chemicals Agency)
- US EPA CompTox Chemicals Dashboard
- Common Chemistry (CAS resource)
- PAN Pesticides Database

Prior to inclusion in the search term string, all forms of chemical names were subjected to verification from several potential sources (*e.g.*, US EPA Chemistry Dashboard, STN International-CAS; see complete list of sources for chemical verification in Table_Apx A-1). From these sources, all chemical names, synonyms, CAS number(s), trade names, etc. were documented and used to generate terms for database searches.

Table_Apx A-1. Sources of Verification for Chemical Names and Structures

Chemical Source	Contents	Document Location
Chemistry Dashboard	CAS Numbers, Synonyms, Structures, Properties, Environmental Fate and Transport.	Online
Dictionary of Chemical Names and Synonyms	Wide assortment of chemical compounds by chemical name and synonym, has CAS index and some structure data	ECOTOX
Farm Chemicals Handbook-1992	Pesticide information, CAS numbers and synonyms, some structure data[a]	ECOTOX
OPPT SMILES Verification Source	Structure data	Electronic verification
RTECS (Registry of Toxic Effects of chemical substance, 1983-84 ed., 2 vols)	Chemical names, synonyms, and CAS numbers	ECOTOX
Sigma – Aldrich website	Organic and inorganic Compounds by chemical name, has CAS index and some structure and Physical Property data	Online
STN International (CAS) 1994	Most complete source of chemical name, synonym and structure information, no physical properties	Online

Chemical Source	Contents	Document Location
The Pesticide Manual 10th edition, 1994	Pesticide compounds by chemical name, synonym, product code, has CAS index and some structure and physical property data	ECOTOX
TSCA Chemical Substance Inventory, 1985 ed., 5 vols)	Chemical names, synonyms, and CAS numbers	ECOTOX
World Wide Web (misc. web sources) A copy of the verification page is saved to the Attachments tab of the chemical entry. This includes company MSDS sheets or Chemical Labels.	Chemical names, synonyms, and CAS numbers	Online
California Department of Pesticide Regulation	Multiple databases containing chemicals, pesticides, companies, products, etc.	Online
PAN Pesticide Database	Pesticides searchable by name or CAS #. Includes CAS #, name, synonyms, targets, toxicity data, related chemicals, and regulatory information.	Online
US EPA Office of Pesticide Programs Pesticide Fate Database – No web access available. An electronic copy of the data file is located at the Contractor site: PFATE_37_Tables.mdb.	Multiple databases containing chemicals, pesticides, companies, products, etc.	Online
[a] Sometimes CAS number presented for a compound is for the main constituent only		

A.1.2 Publicly Available Database Searches

The databases listed below were searched for literature containing the chemical search terms. An information specialist conducted database searching during September 2020 for D4 and during January 2021 for the four degredation products described in Section 2.3.2. The results were stored in the Health and Environmental Research Online (HERO) database and assigned a HERO reference identification number.[7] The present literature search focused only on the chemical name (including synonyms and trade names) with no additional limits. Full details of the search strategy for each database are presented in Appendix A.1.2.1.

After initial deduplication in HERO,[8] these studies were imported into SWIFT Review software (Howard et al., 2016) to identify those references most likely to be applicable to each discipline area (*i.e.*, consumer, environmental, and general population exposure, occupational exposure and environmental releases, environmental hazards, human health hazards, and fate and physical chemistry).

[7] EPA's HERO database provides access to the scientific literature behind EPA science assessments. The database includes more than 600,000 scientific references and data from the peer-reviewed literature used by EPA to develop its regulations.
[8] Deduplication in HERO involves first determining whether a matching unique ID exists (*e.g.*, PMID, WOSid, or DOI). If one matches one that already exists in HERO, HERO will tag the existing reference instead of adding the reference again. Second, HERO checks if the same journal, volume, issue, and page number are already in HERO. Third, HERO matches on the title, year, and first author. Title comparisons ignore punctuation and case.

A.1.2.1 Query Strings for the Publicly Available Database Searches on D4

These are the search terms compiled for Octamethylcyclotetrasiloxane (D4) used in the initial search strategies for each of the databases listed below:

"Octamethylcyclotetrasiloxane" OR ("D4" AND "siloxane") OR "556-67-2" OR "OMCTS" OR "cyclotetrasiloxane" OR "Silbione" OR "Octamethylcyclotetrasiloxan" OR "VS 7207" OR "Cyclotetrasiloxane, octamethyl-" OR "Cyclic dimethylsiloxane tetramer" OR "Dow Corning 344" OR "Volasil 244" OR "DC 244" OR "DC 344" OR "Octamethylcyclotetrasiloxanes"

Table_Apx A-2. Summary of Data Sources, Search Dates and Number of Peer-Reviewed Literature Search Results for Octamethylcyclotetrasiloxane (D4)

Source	Source-Specific Search Strategy	Results
Agricola Search Date: 9/4/2020	ALL("Octamethylcyclotetrasiloxane" OR ("D4" AND "siloxane") OR "556-67-2" OR "OMCTS" OR "cyclotetrasiloxane" OR "Silbione" OR "Octamethylcyclotetrasiloxan" OR "VS 7207" OR "Cyclotetrasiloxane, octamethyl-" OR "Cyclic dimethylsiloxane tetramer" OR "Dow Corning 344" OR "Volasil 244" OR "DC 244" OR "DC 344" OR "Octamethylcyclotetrasiloxanes")	167
Current Contents Search Date: 9/4/2020	(TS="Octamethylcyclotetrasiloxane" OR (TS="D4" AND TS="siloxane") OR TS="556-67-2" OR TS="OMCTS" OR TS="cyclotetrasiloxane" OR TS="Silbione" OR TS="Octamethylcyclotetrasiloxan" OR TS="VS 7207" OR TS="Cyclotetrasiloxane, octamethyl-" OR TS="Cyclic dimethylsiloxane tetramer" OR TS="Dow Corning 344" OR TS="Volasil 244" OR TS="DC 244" OR TS="DC 344" OR TS="Octamethylcyclotetrasiloxanes")	801
ProQuest Dissertations & Theses Search Date: 9/4/2020	ALL("Octamethylcyclotetrasiloxane" OR ("D4" AND "siloxane") OR "556-67-2" OR "OMCTS" OR "cyclotetrasiloxane" OR "Silbione" OR "Octamethylcyclotetrasiloxan" OR "VS 7207" OR "Cyclotetrasiloxane, octamethyl-" OR "Cyclic dimethylsiloxane tetramer" OR "Dow Corning 344" OR "Volasil 244" OR "DC 244" OR "DC 344" OR "Octamethylcyclotetrasiloxanes")	4
ProQuest Agricultural & Scientific Database Search Date: 9/4/2020	ALL("Octamethylcyclotetrasiloxane" OR ("D4" AND "siloxane") OR "556-67-2" OR "OMCTS" OR "cyclotetrasiloxane" OR "Silbione" OR "Octamethylcyclotetrasiloxan" OR "VS 7207" OR "Cyclotetrasiloxane, octamethyl-" OR "Cyclic dimethylsiloxane tetramer" OR "Dow Corning 344" OR "Volasil 244" OR "DC 244" OR "DC 344" OR "Octamethylcyclotetrasiloxanes")	306
PubMed Search Date: 9/4/2020	("Octamethylcyclotetrasiloxane"[tw] OR ("D4"[tw] AND "siloxanes"[MeSH]) OR "556-67-2"[rn] OR "OMCTS"[tw] OR "cyclotetrasiloxane"[tw] OR "Silbione"[tw] OR "Octamethylcyclotetrasiloxan"[tw] OR "VS 7207"[tw] OR "Cyclotetrasiloxane, octamethyl-"[tw] OR "Cyclic dimethylsiloxane tetramer"[tw] OR "Dow Corning 344"[tw] OR "Volasil 244"[tw] OR "DC 244"[tw] OR "DC 344"[tw] OR "Octamethylcyclotetrasiloxanes"[tw])	259
Science Direct	1. ("Octamethylcyclotetrasiloxane" OR ("D4" AND "siloxane") OR "556-67-2" OR "OMCTS" OR "cyclotetrasiloxane" OR "Silbione" OR "Octamethylcyclotetrasiloxan")	405

Source	Source-Specific Search Strategy	Results
Search Date: 9/4/2020	2. ("VS 7207" OR "Cyclotetrasiloxane, octamethyl-" OR "Cyclic dimethylsiloxane tetramer" OR "Dow Corning 344" OR "Volasil 244" OR "DC 244" OR "DC 344" OR "Octamethylcyclotetrasiloxanes")	
ToxLine Search Date: 9/4/2020	1. ALL("Octamethylcyclotetrasiloxane" OR ("D4" AND "siloxane") OR "556-67-2" OR "OMCTS" OR "cyclotetrasiloxane" OR "Silbione" OR "Octamethylcyclotetrasiloxan" OR "VS 7207" OR "Cyclotetrasiloxane, octamethyl-" OR "Cyclic dimethylsiloxane tetramer" OR "Dow Corning 344" OR "Volasil 244" OR "DC 244" OR "DC 344" OR "Octamethylcyclotetrasiloxanes") 2. tox [subset] AND ("Octamethylcyclotetrasiloxane"[tw] OR ("D4"[tw] AND "siloxanes"[MeSH]) OR "556-67-2"[rn] OR "OMCTS"[tw] OR "cyclotetrasiloxane"[tw] OR "Silbione"[tw] OR "Octamethylcyclotetrasiloxan"[tw] OR "VS 7207"[tw] OR "Cyclotetrasiloxane, octamethyl-"[tw] OR "Cyclic dimethylsiloxane tetramer"[tw] OR "Dow Corning 344"[tw] OR "Volasil 244"[tw] OR "DC 244"[tw] OR "DC 344"[tw] OR "Octamethylcyclotetrasiloxanes"[tw])	197
WoS Search Date: 9/4/2020	(TS="Octamethylcyclotetrasiloxane" OR (TS="D4" AND TS="siloxane") OR TS="556-67-2" OR TS="OMCTS" OR TS="cyclotetrasiloxane" OR TS="Silbione" OR TS="Octamethylcyclotetrasiloxan" OR TS="VS 7207" OR TS="Cyclotetrasiloxane, octamethyl-" OR TS="Cyclic dimethylsiloxane tetramer" OR TS="Dow Corning 344" OR TS="Volasil 244" OR TS="DC 244" OR TS="DC 344" OR TS="Octamethylcyclotetrasiloxanes")	1,162
Total	**Represents totals across all databases after deduplication.**	**1,533**

Additional Strategies

Additional keywords have been searched to supplement the primary pool references. The supplemental search was performed on four degradants during January 2021. These are the search terms used in the supplemental search strategies for each of the databases listed below:

1. *Octamethyltetrasiloxanediol:* Octamethyltetrasiloxanediol; 3081-07-0; 1,7-Tetrasiloxanediol, 1,1,3,3,5,5,7,7-octamethyl-; Octamethyltetrasiloxane-1,7-diol; Tetrasiloxane-1,7-diol, 1,1,3,3,5,5,7,7-octamethyl-
2. *Hexamethyltrisiloxanediol:* Hexamethyltrisiloxanediol; 3663-50-1; 1,5-Trisiloxanediol, 1,1,3,3,5,5-hexamethyl-; Hexamethyltrisiloxane-1,5-diol
3. *Tetramethyldisiloxanediol:* Tetramethyldisiloxanediol; 1118-15-6; Tetramethyldisiloxane-1,3-diol; 1,3-Disiloxanediol, 1,1,3,3-tetramethyl-
4. *Dimethylsilanediol:* Dimethylsilanediol; 1066-42-8; Dimethyldihydroxysilane; Dihydroxydimethylsilane; Silanediol, dimethyl-

Table_Apx A-3. Summary of Supplemental Data Sources, Search Dates, and Number of Peer-Reviewed Literature Search Results for Octamethylcyclotetrasiloxane (D4)

Source	Source-Specific Search Strategy	Results
Agricola Search Date:	TIAB("Octamethyltetrasiloxanediol" OR "3081-07-0" OR "1,7-Tetrasiloxanediol, 1,1,3,3,5,5,7,7-octamethyl-" OR "Octamethyltetrasiloxane-1,7-diol" OR "Tetrasiloxane-1,7-diol, 1,1,3,3,5,5,7,7-octamethyl-" OR	0

Source	Source-Specific Search Strategy	Results
1/13/2021	"Hexamethyltrisiloxanediol" OR "3663-50-1" OR "1,5-Trisiloxanediol, 1,1,3,3,5,5-hexamethyl-" OR "Hexamethyltrisiloxane-1,5-diol" OR "Tetramethyldisiloxanediol" OR "1118-15-6" OR "Tetramethyldisiloxane-1,3-diol" OR "1,3-Disiloxanediol, 1,1,3,3-tetramethyl-" OR "Dimethylsilanediol" OR "1066-42-8" OR "Dimethyldihydroxysilane" OR "Dihydroxydimethylsilane" OR "Silanediol, dimethyl-")	
Current Contents Search Date: 1/13/2021	TS=("Octamethyltetrasiloxanediol" OR "3081-07-0" OR "1,7-Tetrasiloxanediol, 1,1,3,3,5,5,7,7-octamethyl-" OR "Octamethyltetrasiloxane-1,7-diol" OR "Tetrasiloxane-1,7-diol, 1,1,3,3,5,5,7,7-octamethyl-" OR "Hexamethyltrisiloxanediol" OR "3663-50-1" OR "1,5-Trisiloxanediol, 1,1,3,3,5,5-hexamethyl-" OR "Hexamethyltrisiloxane-1,5-diol" OR "Tetramethyldisiloxanediol" OR "1118-15-6" OR "Tetramethyldisiloxane-1,3-diol" OR "1,3-Disiloxanediol, 1,1,3,3-tetramethyl-" OR "Dimethylsilanediol" OR "1066-42-8" OR "Dimethyldihydroxysilane" OR "Dihydroxydimethylsilane" OR "Silanediol, dimethyl-")	0
ProQuest Dissertations & Theses Search Date: 1/13/2021	TIAB("Octamethyltetrasiloxanediol" OR "3081-07-0" OR "1,7-Tetrasiloxanediol, 1,1,3,3,5,5,7,7-octamethyl-" OR "Octamethyltetrasiloxane-1,7-diol" OR "Tetrasiloxane-1,7-diol, 1,1,3,3,5,5,7,7-octamethyl-" OR "Hexamethyltrisiloxanediol" OR "3663-50-1" OR "1,5-Trisiloxanediol, 1,1,3,3,5,5-hexamethyl-" OR "Hexamethyltrisiloxane-1,5-diol" OR "Tetramethyldisiloxanediol" OR "1118-15-6" OR "Tetramethyldisiloxane-1,3-diol" OR "1,3-Disiloxanediol, 1,1,3,3-tetramethyl-" OR "Dimethylsilanediol" OR "1066-42-8" OR "Dimethyldihydroxysilane" OR "Dihydroxydimethylsilane" OR "Silanediol, dimethyl-")	0
ProQuest Agricultural & Scientific Database Search Date: 1/13/2021	TIAB("Octamethyltetrasiloxanediol" OR "3081-07-0" OR "1,7-Tetrasiloxanediol, 1,1,3,3,5,5,7,7-octamethyl-" OR "Octamethyltetrasiloxane-1,7-diol" OR "Tetrasiloxane-1,7-diol, 1,1,3,3,5,5,7,7-octamethyl-" OR "Hexamethyltrisiloxanediol" OR "3663-50-1" OR "1,5-Trisiloxanediol, 1,1,3,3,5,5-hexamethyl-" OR "Hexamethyltrisiloxane-1,5-diol" OR "Tetramethyldisiloxanediol" OR "1118-15-6" OR "Tetramethyldisiloxane-1,3-diol" OR "1,3-Disiloxanediol, 1,1,3,3-tetramethyl-" OR "Dimethylsilanediol" OR "1066-42-8" OR "Dimethyldihydroxysilane" OR "Dihydroxydimethylsilane" OR "Silanediol, dimethyl-")	48
PubMed Search Date: 1/13/2021	"Octamethyltetrasiloxanediol"[tw] OR "3081-07-0"[rn] OR "1,7-Tetrasiloxanediol, 1,1,3,3,5,5,7,7-octamethyl-"[tw] OR "Octamethyltetrasiloxane-1,7-diol"[tw] OR "Tetrasiloxane-1,7-diol, 1,1,3,3,5,5,7,7-octamethyl-"[tw] OR "Hexamethyltrisiloxanediol"[tw] OR "3663-50-1"[rn] OR "1,5-Trisiloxanediol, 1,1,3,3,5,5-hexamethyl-"[tw] OR "Hexamethyltrisiloxane-1,5-diol"[tw] OR "Tetramethyldisiloxanediol"[tw] OR "1118-15-6"[rn] OR "Tetramethyldisiloxane-1,3-diol"[tw] OR "1,3-Disiloxanediol, 1,1,3,3-tetramethyl-"[tw] OR "Dimethylsilanediol"[tw] OR "1066-42-8"[rn] OR "Dimethyldihydroxysilane"[tw] OR "Dihydroxydimethylsilane"[tw] OR "Silanediol, dimethyl-"[tw]	22
Science Direct Search Date: 1/13/2021	1. "Octamethyltetrasiloxanediol" OR "3081-07-0" OR "1,7-Tetrasiloxanediol, 1,1,3,3,5,5,7,7-octamethyl-" OR "Octamethyltetrasiloxane-1,7-diol" OR "Tetrasiloxane-1,7-diol, 1,1,3,3,5,5,7,7-octamethyl-" OR "Hexamethyltrisiloxanediol" OR "3663-50-1" 2. "1,5-Trisiloxanediol, 1,1,3,3,5,5-hexamethyl-" OR "Hexamethyltrisiloxane-1,5-diol" OR "Tetramethyldisiloxanediol" OR "1118-15-6" OR	0

Source	Source-Specific Search Strategy	Results
	"Tetramethyldisiloxane-1,3-diol" OR "1,3-Disiloxanediol, 1,1,3,3-tetramethyl-" OR "Dimethylsilanediol" OR "1066-42-8" 3. "Dimethyldihydroxysilane" OR "Dihydroxydimethylsilane" OR "Silanediol, dimethyl-"	
ToxLine Search Date: 1/13/2021	1. TIAB("Octamethyltetrasiloxanediol" OR "3081-07-0" OR "1,7-Tetrasiloxanediol, 1,1,3,3,5,5,7,7-octamethyl-" OR "Octamethyltetrasiloxane-1,7-diol" OR "Tetrasiloxane-1,7-diol, 1,1,3,3,5,5,7,7-octamethyl-" OR "Hexamethyltrisiloxanediol" OR "3663-50-1" OR "1,5-Trisiloxanediol, 1,1,3,3,5,5-hexamethyl-" OR "Hexamethyltrisiloxane-1,5-diol" OR "Tetramethyldisiloxanediol" OR "1118-15-6" OR "Tetramethyldisiloxane-1,3-diol" OR "1,3-Disiloxanediol, 1,1,3,3-tetramethyl-" OR "Dimethylsilanediol" OR "1066-42-8" OR "Dimethyldihydroxysilane" OR "Dihydroxydimethylsilane" OR "Silanediol, dimethyl-") 2. tox[subset] AND ("Octamethyltetrasiloxanediol"[tw] OR "3081-07-0"[rn] OR "1,7-Tetrasiloxanediol, 1,1,3,3,5,5,7,7-octamethyl-"[tw] OR "Octamethyltetrasiloxane-1,7-diol"[tw] OR "Tetrasiloxane-1,7-diol, 1,1,3,3,5,5,7,7-octamethyl-"[tw] OR "Hexamethyltrisiloxanediol"[tw] OR "3663-50-1"[rn] OR "1,5-Trisiloxanediol, 1,1,3,3,5,5-hexamethyl-"[tw] OR "Hexamethyltrisiloxane-1,5-diol"[tw] OR "Tetramethyldisiloxanediol"[tw] OR "1118-15-6"[rn] OR "Tetramethyldisiloxane-1,3-diol"[tw] OR "1,3-Disiloxanediol, 1,1,3,3-tetramethyl-"[tw] OR "Dimethylsilanediol"[tw] OR "1066-42-8"[rn] OR "Dimethyldihydroxysilane"[tw] OR "Dihydroxydimethylsilane"[tw] OR "Silanediol, dimethyl-"[tw])	10
WoS Search Date: 1/13/2021	TS=("Octamethyltetrasiloxanediol" OR "3081-07-0" OR "1,7-Tetrasiloxanediol, 1,1,3,3,5,5,7,7-octamethyl-" OR "Octamethyltetrasiloxane-1,7-diol" OR "Tetrasiloxane-1,7-diol, 1,1,3,3,5,5,7,7-octamethyl-" OR "Hexamethyltrisiloxanediol" OR "3663-50-1" OR "1,5-Trisiloxanediol, 1,1,3,3,5,5-hexamethyl-" OR "Hexamethyltrisiloxane-1,5-diol" OR "Tetramethyldisiloxanediol" OR "1118-15-6" OR "Tetramethyldisiloxane-1,3-diol" OR "1,3-Disiloxanediol, 1,1,3,3-tetramethyl-" OR "Dimethylsilanediol" OR "1066-42-8" OR "Dimethyldihydroxysilane" OR "Dihydroxydimethylsilane" OR "Silanediol, dimethyl-")	79
Total	**Represents totals across all databases after deduplication.**	**96**

A.1.2.2 Data Prioritization for Environmental Hazard, Human Health Hazard, Fate and Physical Chemistry

In brief, SWIFT Review has pre-set literature search strategies ("filters") developed by information specialists that can be applied to identify studies that are more likely to be useful for identifying human health and ecotoxicity content from those that likely do not (*e.g.*, analytical methods). The filters function like a typical search strategy where studies are tagged as belonging to a certain filter if the terms in the filter literature search strategy appear in title, abstract, keyword or medical subject headings (MeSH*)* fields content. The applied SWIFT Review filters focused on lines of evidence: human, animal models for human health, ecological taxa (which includes ecotoxicological animal models, plants, and other taxa), and *in vitro* studies. The details of the search strategies that underlie the filters are available online. Studies not retrieved using these filters were not considered further. Studies that included one or

more of the search terms in the title, abstract, keyword, or MeSH fields were exported as a RIS file for screening in Swift-ActiveScreener or DistillerSR.[9]

A.1.2.3 Data Prioritization for Occupational Exposures and Environmental Releases and Gen Pop, Consumer, and Environmental Exposures

To prioritize references related to occupational exposure, environmental release, general population exposure, consumer exposure, and environmental exposure, EPA used positive and negative seed studies to build a classification model in SWIFT Review. The positive seeds were identified using relevant literature pool for the first ten TSCA risk evaluations, while the negative seeds were identified from a subset of literature for the current high-priority substances. The model was then applied to the unclassified literature to generate a classification score for each reference. Scores above a certain threshold value were then prioritized for further review in SWIFT-ActiveScreener.

A.2 Peer-Reviewed Screening Process

The studies identified from publicly available database searches and SWIFT-Review filtering/prioritization were housed in HERO system and imported into SWIFT-ActiveScreener or DistillerSR for title/abstract and full-text screening. Both title/abstract and full-text screening were conducted by two independent reviewers. Screening is initiated with a pilot phase of screening (between 10 and 50) studies to identify areas where clarification in screening criteria might be needed or chemical-specific supplemental material tags might be identified. Records that met PECO (or equivalent criteria (Appendix A.2.1) during title and abstract screening were considered for full-text screening. At both the title/abstract and full-text review levels, screening conflicts were resolved by topic-specific experts and/or discussion among the primary screeners. For citations with no abstract, the articles are initially screened based on all or some of the following: title relevance (titles that suggest a record is not relevant can be excluded rather than marked as unclear), and page numbers (articles two pages in length or less were assumed to be conference reports, editorials, or letters). During title/abstract or full-text level screening in DistillerSR, studies that did not meet the PECO criteria, but which could provide supporting information were categorized (or "tagged") as supplemental information.

It is important to emphasize that being tagged as supplemental material does not mean the study would necessarily be excluded from consideration in an assessment. The initial screening level distinctions between a study meeting the PECO criteria and a supplemental study are often made for practical reasons and the tagging structures (as seen in the literature inventory trees and heat maps in Section 2.1 of this document) are designed to ensure the supplemental studies are categorized for easy retrieval if needed while conducting the assessment. The impact on the assessment conclusions of individual studies tagged as supporting material is often difficult to assess during the screening phase of the assessment. These studies may emerge as being critically important to the assessment and need to be evaluated and summarized at the individual study level (*e.g.*, cancer MOA mechanistic or non-English-language studies), or be helpful to provide context (*e.g.*, summarize current levels of exposure, provide hazard evidence from routes or durations of exposure not pertinent to the PECO), or not be cited at all in the assessment (*e.g.*, individual studies that contribute to a well-established scientific conclusion). Studies maybe be tagged as supplemental material during either title and abstract or full-text screening. When tagged as supplemental material during title and abstract screening, it may not be completely clear whether the chemical of interest is reported in the study (*i.e.*, abstracts may not describe all chemicals investigated). In these cases, studies are still tagged with the expectation that if full-text retrieval is pursued, then additional screening would be needed to clarify if the study is pertinent.

[9] DistillerSR is a web-based systematic review software used to screen studies.

A.2.1 Inclusion/Exclusion Criteria

A PECO statement is typically used to focus the research question(s), search terms, and inclusion/exclusion criteria in a systematic review. PECO criteria were developed *a priori* to screening and modified to fit the various discipline areas supporting the TSCA risk evaluations. Variations include the RESO (receptor, exposure, scenario/setting, and outcome) used for the occupational exposure and environmental releases discipline, and PESO (pathways/processes, exposures, setting/scenario, and outcomes) used by the fate and transport discipline. All PECOs and PECO-equivalent criteria can be found in the following sections.

A.2.1.1 PECO for Environmental and Human Health Hazards

The PECO used in this evidence map to identify literature pertinent to D4 effects on human health and environmental hazard is presented in Table_Apx A-4. In addition to the PECO criteria, studies containing potentially relevant supplemental material were tracked and categorized during the literature screening process as outlined in Table_Apx A-5.

Table_Apx A-4. Hazards Title and Abstract and Full-Text PECO Criteria for D4

PECO Element	Evidence
Population	• **Human:** Any population and life stage (*e.g.*, occupational or general population, including children and other sensitive populations). • **Animal:** Aquatic and terrestrial species (live, whole organism) from any life stage (*e.g.*, preconception, in utero, lactation, peripubertal, and adult stages). Animal models will be inventoried according to the categorization below: – Human health models: rat, mouse, rabbit, dog, hamster, guinea pig, cat, non-human primate, pig, hen (neurotoxicity only) – Ecotoxicological models: invertebrates (*e.g.*, insects, spiders, crustaceans, mollusks, and worms) and vertebrates (*e.g.*, mammals and all amphibians, birds, fish, and reptiles). All hen studies (including neurotoxicity studies) will be included for ecotoxicological models. • **Plants:** All aquatic and terrestrial species (live), including algal, moss, lichen, and fungi species. **Screener note:** • To identify human health and environmental hazards, other organisms not listed above in their respective categories can also be used. Non-mammalian model systems are increasingly used to identify potential human health hazards (*e.g.*, Xenopus, zebrafish), and traditional human health models (*e.g.*, rodents) can be used to identify potential environmental hazard. Neurotoxicity studies performed in hens (*e.g.*, OECD 418 and 419) are considered relevant to both human and eco hazard • PECO considerations should be directed toward effects on target species only and not on the indirect effects expressed in taxa as a result of chemical treatment (*e.g.*, substance is lethal to a targeted pest species leading to positive effects on plant growth due to diminished presence of the targeted pest species). • Tests of the single toxicants in in vitro and ex vivo systems or on gametes, embryos, or plant or fungal sections capable of forming whole, new organisms will be tagged as potentially supplemental (mechanistic studies). Bacteria and yeast studies specific for assessing genotoxicity or mutagenicity (*e.g.*, Ames assay) will also be tagged as potentially supplemental (mechanistic studies) but are otherwise excluded. Studies on viruses are excluded.

PECO Element	Evidence
Exposure	**Relevant forms and isomers:** Octamethylcyclotetrasiloxane (D4); CASRN: 556-67-2 • No **isomers** were included for D4 For **synonyms** see a list of validated synonyms on the EPA Chemistry Dashboard • **Human:** Any exposure to Octamethylcyclotetrasiloxane (D4); CASRN: 556-67-2 singularly or in mixture, including exposure as measured by internal concentrations of these chemicals or metabolites of these chemicals in a biological matrix (*i.e.*, urine, blood, semen, etc.). • **Animal:** Any exposure to Octamethylcyclotetrasiloxane (D4); CASRN: 556-67-2 including via water (including environmental aquatic exposures), soil or sediment, diet, gavage, injection, dermal, and inhalation. • **Plants:** Any exposure to Octamethylcyclotetrasiloxane (D4); CASRN: 556-67-2 including via water, soil, sediment. **Screener note:** • Field studies with media concentrations (*e.g.*, surface water, interstitial water, soil, sediment) and/or body/tissue concentrations of animals or plants are to be identified as *Supplemental* if any biological effects are reported. • Studies involving exposures to mixtures will be included only if they also include exposure to Octamethylcyclotetrasiloxane (D4); CASRN: 556-67-2 alone. Otherwise, mixture studies will be tagged as *Supplemental*. • Controlled outdoor experimental studies (*e.g.*, controlled crop/greenhouse studies, mesocosm studies, artificial stream studies) are considered to be laboratory studies (not field studies) because there is a known and prescribed exposure dose(s) and an evaluation of hazardous effect(s). Whereas field studies (*e.g.*, biomonitoring) where there is no prescribed exposure dose(s) will be *excluded* if there is no evaluated hazardous effect, and tagged as supplemental field, if there is an evaluated hazardous effect. • D4 degradants (4) and other relevant siloxane structures (6) are also identified and should be tagged as supplemental if PECO-relevant.
Comparator	• **Human:** A comparison or referent population exposed to lower levels (or no exposure/exposure below detection limits) of Octamethylcyclotetrasiloxane (D4); CASRN: 556-67-2, or exposure to Octamethylcyclotetrasiloxane (D4); CASRN: 556-67-2 for shorter periods of time. • **Animal and Plants:** A concurrent control group exposed to vehicle-only treatment and/or untreated control (control could be a baseline measurement). **Screener note:** • If no control group is explicitly stated or implied (*e.g.*, by mention of statistical results that could only be obtained if a control group was present), the study will be marked as *Unclear* during Title/Abstract Screening. • All case series and case reports describing findings in a sample size of less than 20 people in any setting (*e.g.*, occupation, general population) will be tracked as *Supplemental*. • Case-control, case-crossover, case-referent, case-only, case-specular, case-cohort, case-parent, cross sectional, nested case-control study designs are all *Included.*

PECO Element	Evidence
Outcomes	• **Human:** All health outcomes (cancer and non-cancer) at the organ level or higher. • **Animal and Plants:** All apical biological effects (effects measured at the organ level or higher) and bioaccumulation from laboratory studies with concurrently measured media and/or tissue concentrations). Apical endpoints include but are not limited to reproduction, survival, and growth. **Screener note:** • Measurable biological effects relevant for humans, animals and plants may include but are not limited to mortality, behavioral, population, cellular, physiological, growth, reproduction, systemic, point of contact (irritation and sensitization) effects. • Effects measured at the cellular level of biological organization and below are to be tagged as supplemental, mechanistic.

Table_Apx A-5. Major Categories of "Potentially Relevant" Supplemental Materials for D4

Category	Evidence
Mechanistic studies	All studies that report results at the cellular level and lower in both mammalian and non-mammalian model systems, including *in vitro*, *in vivo*, *ex vivo*, and *in silico* studies. These studies include assays for genotoxicity or mutagenicity using bacteria or yeast.
ADME, PBPK, and toxicokinetic	Studies designed to capture information regarding ADME, toxicokinetic studies, or physiologically based pharmacokinetic (PBPK) models.
Case reports or case series	Case reports ($n \leq 3$ cases) and case series (non-occupational) will be tracked as potentially relevant supplemental information.
Potentially exposed or susceptible subpopulations (no health outcome)	Studies that identify potentially susceptible subgroups; for example, studies that focus on a specific demographic, life stage, or genotype. This tag applies primarily during full-text screening. **Screener note:** If biological susceptibility issues are clearly present or *strongly* implied in the title/abstract, this supplemental tag may be applied at the title abstract level. If uncertain at title/abstract, do not apply this tag to the reference during title/abstract screening.
Mixture studies	Experimental mixture studies that are not considered PECO-relevant because they do not contain an exposure or treatment group assessing only the chemical of interest. Human health animal model and environmental animal model/plant will be tagged separately for mixture studies.
Records with no original data	Records that do not contain original data, such as other agency assessments, informative scientific literature reviews, editorials, or commentaries.
Conference abstracts	Records that do not contain sufficient documentation to support study evaluation and data extraction.

Category	Evidence
Non-English records	Non-English records will be tracked as potentially relevant supplemental information.
Field studies	Field studies with media concentrations (*e.g.*, surface water, interstitial water, soil, sediment) and/or body/tissue concentrations of animals or plants if biological effects reported.
Other relevant chemical structures	PECO-relevant studies with other chemical structures such as metabolites or degradants that may be useful later. For example, identified degradants for D4 include octamethyltetrasiloxanediol (CASRN 3081-07-0), hexamethyltrisiloxanediol (CASRN 3663-50-1), tetramethyldisiloxanediol (CASRN 1118-15-6) and dimethylsilanediol (CASRN 1066-42-8). In addition, six other relevant siloxane structures, should also be tagged as supplemental: octamethyltrisiloxane (L3), decamethyltetrasiloxane (L4), dodecamethylpentasiloxane (L5), hexamethylcyclotrisiloxane (D3), decamethylcyclopentasiloxane (D5) and dodecamethylcyclohexasiloxane (D6).

A.2.1.2 PECO for Consumer, Environmental, and General Population Exposures.

Table_Apx A-6. Generic Inclusion Criteria for the Data Sources Reporting Exposure Data on General Population, Consumers, and Environmental Receptors

PECO Element	Evidence
Population	**Human:** General population; consumers; bystanders in the home; near-facility populations (includes industrial and commercial facilities manufacturing, processing, or using the chemical substance); children; susceptible populations (life stages, preexisting conditions, genetic factors), pregnant women; lactating women, women of child-bearing age. Many human population groups may be exposed. No chemical-specific exclusions are suggested at this time.
	Environmental: Aquatic species, terrestrial species, terrestrial plants, aquatic plants (field studies only)
Exposure	**Expected Primary Exposure Sources, Pathways, Routes:** Pathways: indoor air/vapor/mist; indoor dust; particles; outdoor/ambient air; surface water; biosolids; sediment; human milk; food items containing D4 including fish; consumer product uses in the home (including consumer product containing chemical) Routes of Exposure: Inhalation, Oral, Dermal
Comparator (Scenario)	**Human:** Consider media-specific background exposure scenarios and use/source specific exposure scenarios as well as which receptors are and are not reasonably exposed across the projected exposure scenarios.

PECO Element	Evidence
	Environmental: Consider media-specific background exposure scenarios and use/source specific exposure scenarios as well as which receptors are and are not reasonably exposed across the projected exposure scenarios.
Outcomes for Exposure Concentration or Dose	**Human:** Acute, subchronic, and/or indoor air and water concentration estimates (mg/m^3 or mg/L). Both external potential dose and internal dose based on biomonitoring and reverse dosimetry mg/kg/day will be considered. Characteristics of consumer products or articles (weight fraction, emission rates, etc) containing D4.
	Environmental: A wide range of ecological receptors will be considered (range depending on available ecotoxicity data) using surface water concentrations, sediment concentrations.

Table_Apx A-7. Pathways Identified as Supplemental for D4[a]

Chemical	Drinking Water	Ambient Air	Air Disposal	Land Disposal	Underground Disposal	Groundwater
D4	–	–	–	–	–	–

[a] "Supplemental pathways" refer to pathways addressed by other EPA administered statutes. Studies tagged under these pathways provide media information that is not prioritized in the screening process

A.2.1.3 RESO for Occupational Exposure and Environmental Releases

EPA developed a generic RESO statement to guide the screening of engineering and occupational exposure data or information sources for the TSCA risk evaluations. Data or information sources that comply with the inclusion criteria specified in the RESO statement are eligible for inclusion, considered for evaluation, and possibly included in the environmental release and occupational exposure assessments. On the other hand, data or information sources that fail to meet the criteria in the RESO statement are excluded from further consideration.

Assessors seek information on various chemical-specific engineering and occupational exposure data needs as part of the process of developing the exposure assessment for each risk evaluation. EPA uses the RESO statement (Table_Apx A-8) along with the information in Table_Apx A-9 when screening the engineering and occupational exposure data and information.

Table_Apx A-8. Inclusion Criteria for Data Sources Reporting Engineering and Occupational Exposure Data

RESO Element	Evidence
Receptors	• Humans: Workers, including occupational non-users • Environment: All environmental receptors (relevant release estimates input to Exposure)

RESO Element	Evidence
	Please refer to the conceptual models for more information about the environmental and human receptors included in the TSCA risk evaluation.
Exposure	• Worker exposure to and relevant environmental releases of the chemical substance from occupational scenarios: Dermal and inhalation exposure routes (as indicated in the conceptual model) Oral route (as indicated in the conceptual model) Please refer to the conceptual models for more information about the routes and media/pathways included in the TSCA risk evaluation.
Setting or **S**cenario	• Any occupational setting or scenario resulting in worker exposure and relevant environmental releases (includes all manufacturing, processing, use, disposal).
Outcomes	• Quantitative estimates[a] of worker exposures and of relevant environmental releases from occupational settings • General information and data related and relevant to the occupational estimates[a]
[a] Metrics (*e.g.*, mg/kg/day or mg/m^3 for worker exposures, kg/site/day for releases) are determined by toxicologists for worker exposures and by exposure assessors for releases; also, the Engineering, Release and Occupational Exposure Data Needs (Table_Apx A-9) provides a list of related and relevant general information.	

Table_Apx A-9. Engineering, Environmental Release and Occupational Data Necessary to Develop the Environmental Release and Occupational Exposure Assessments

Objective Determined during Scoping	Type of Data[a]
General Engineering Assessment (may apply to Occupational Exposures and / or Environmental Releases)	Description of the life cycle of the chemical(s) of interest, from manufacture to end-of-life (*e.g.*, each manufacturing, processing, or use step), and material flow between the industrial and commercial life cycle stages. The total annual U.S. volume (lb/yr or kg/yr) of the chemical(s) of interest manufactured, imported, processed, and used; and the share of total annual manufacturing and import volume that is processed or used in each life cycle step. Description of processes, equipment, and unit operations during each industrial/ commercial life cycle step. Material flows, use rates, and frequencies (lb/site-day or kg/site-day and days/yr; lb/site-batch and batches/yr) of the chemical(s) of interest during each industrial/ commercial life cycle step. Note: if available, include weight fractions of the chemicals (s) of interest and material flows of all associated primary chemicals (especially water). Number of sites that manufacture, process, or use the chemical(s) of interest for each industrial/ commercial life cycle step and site locations. Concentration of the chemical of interest
Occupational Exposures	Description of worker activities with exposure potential during the manufacture, processing, or use of the chemical(s) of interest in each industrial/commercial life cycle stage. Potential routes of exposure (*e.g.*, inhalation, dermal). Physical form of the chemical(s) of interest for each exposure route (*e.g.*, liquid, vapor, mist) and activity.

Objective Determined during Scoping	Type of Data[a]
	Breathing zone (personal sample) measurements of occupational exposures to the chemical(s) of interest, measured as time-weighted averages (TWAs), short-term exposures, or peak exposures in each occupational life cycle stage (or in a workplace scenario similar to an occupational life cycle stage). Area or stationary measurements of airborne concentrations of the chemical(s) of interest in each occupational setting and life cycle stage (or in a workplace scenario similar to the life cycle stage of interest). For solids, bulk and dust particle size characterization data. Dermal exposure data. Exposure duration (hr/day). Exposure frequency (days/yr). Number of workers who potentially handle or have exposure to the chemical(s) of interest in each occupational life cycle stage. PPE types employed by the industries within scope. Engineering Controls employed to reduce occupational exposures in each occupational life cycle stage (or in a workplace scenario similar to the life cycle stage of interest), and associated data or estimates of exposure reductions.
Environmental Releases (to relevant environmental media)	Description of sources of potential environmental releases, including cleaning of residues from process equipment and transport containers, involved during the manufacture, processing, or use of the chemical(s) of interest in each life cycle stage. Estimated mass (lb or kg) of the chemical(s) of interest released from industrial and commercial sites to each environmental medium (water) and treatment and disposal methods (POTW), including releases per site and aggregated over all sites (annual release rates, daily release rates) Release or emission factors. Number of release days per year. Waste treatment methods and pollution control devices employed by the industries within scope and associated data on release/emission reductions.
In addition to the data types listed above, EPA may identify additional data needs for mathematical modeling. These data needs will be determined on a case-by-case basis. [a] These are the tags included in the full-text screening form. The screener makes a selection from these specific tags, which describe more specific types of data or information.	

A.2.1.4 PESO for Fate and Transport

EPA developed a generic PESO statement to guide the screening of environmental fate data or information sources for the TSCA risk evaluations. Data or information sources that comply with the inclusion criteria in the PESO statement are eligible for inclusion, considered for evaluation, and possibly included in the environmental fate assessment. On the other hand, data or information sources that fail to meet the criteria in the PESO statement are excluded from further consideration.

Assessors seek information on various chemical-specific fate endpoints and associated fate processes, environmental media, and exposure pathways as part of the process of developing the environmental fate assessment for each risk evaluation. EPA uses the PESO statement (Table_Apx A-10) along with the information in Table_Apx A-11 when screening the fate data or information sources to ensure complete coverage of the processes, pathways and data or information relevant to the environmental fate and transport of the chemical substance undergoing risk evaluation.

Table_Apx A-10. Inclusion Criteria for Data or Information Sources Reporting Environmental Fate and Transport Data

PESO Element	Evidence
Pathways and **P**rocesses	Environmental fate, transport, partitioning and degradation behavior across environmental media to inform exposure pathways of the chemical category of interest Exposure pathways included in the conceptual models: air, surface water, groundwater, wastewater, soil, sediment and biosolids. Processes associated with the target exposure pathways Bioconcentration and bioaccumulation Destruction and removal by incineration Please refer to the conceptual models for more information about the exposure pathways included in each TSCA risk evaluation.
Exposure	Environmental exposure of environmental receptors (i.e., aquatic and terrestrial organisms) to the chemical substance of interest, mixtures including the chemical substance, and/or its degradation products and metabolites Environmental exposure of human receptors, including any PESS, to the chemical substance of interest, mixtures including the chemical substance, and/or its degradation products and metabolites Please refer to the conceptual models for more information about the
Setting or Scenario	Any setting or scenario resulting in releases of the chemical substance of interest into the natural or built environment (e.g., buildings including homes or workplaces, or wastewater treatment facilities) that would expose environmental (i.e., aquatic and terrestrial organisms) or human receptors (i.e., general population and PESS)
Outcomes	Fate properties which allow assessments of exposure pathways: Abiotic and biotic degradation rates, mechanisms, pathways, and products Bioaccumulation magnitude and metabolism rates Partitioning within and between environmental media (see Pathways and Processes)

Table_Apx A-11. Fate Endpoints and Associated Processes, Media, and Exposure Pathways Considered in the Development of the Environmental Fate Assessment

Fate Data Endpoint	Associated Process(es)	Associated Media/Exposure Pathways			
		Surface Water, Wastewater, Sediment	Soil, Biosolids	Groundwater	Air
Required environmental fate data					
Abiotic reduction rates or half-lives	Abiotic reduction, Abiotic dehalogenation	X			

Fate Data Endpoint	Associated Process(es)	Associated Media/Exposure Pathways			
		Surface Water, Wastewater, Sediment	Soil, Biosolids	Groundwater	Air
Aerobic biodegradation rates or half-lives	Aerobic biodegradation	X	X		
Anaerobic biodegradation rates or half-lives	Anaerobic biodegradation	X	X	X	
Aqueous photolysis (direct and indirect) rates or half-lives	Aqueous photolysis (direct and indirect)	X			
Atmospheric photolysis (direct and indirect) rates or half-lives	Atmospheric photolysis (direct and indirect)				X
Bioconcentration factor (BCF), Bioaccumulation factor (BAF)	Bioconcentration, Bioaccumulation	X	X		X
Biomagnification and related information	Trophic magnification	X			
Desorption information	Sorption, Mobility	X	X	X	
Destruction and removal by incineration	Incineration				X
Hydrolysis rates or half-lives	Hydrolysis	X	X	X	
K_{OC} and other sorption information	Sorption, Mobility	X	X	X	
Wastewater treatment removal information	Wastewater treatment	X	X		
Supplemental (or optional) environmental fate data					
Abiotic transformation products	Hydrolysis, Photolysis, Incineration	X			X
Aerobic biotransformation products	Aerobic biodegradation	X	X		
Anaerobic biotransformation products	Anaerobic biodegradation	X	X	X	
Atmospheric deposition information	Atmospheric deposition				X
Coagulation information	Coagulation, Mobility	X		X	
Incineration removal information	Incineration				X

A.2.1.5 Generation of Hazard Heat Maps

As stated in Appendix A.1.2.2, SWIFT Review has pre-set literature search strategies ("filters") developed by information specialists that can be applied to identify studies that are more likely to be useful for identifying human health and ecotoxicity content. The filters function like a typical search strategy where studies are tagged as belonging to a certain filter if the terms in the filter literature search strategy appear in title, abstract, keyword or MeSH fields content.

After the completion of full-text screening for hazard data, all references tagged as included (or "PECO-relevant) were uploaded to the SWIFT Review tool for further filtering. The SWIFT Review filters applied at this phase focused on types of health outcomes included: "ADME", "PBPK", "cancer", "cardiovascular", "developmental", "endocrine", "gastrointestinal", "hematological and immune", "hepatic", "mortality", "musculoskeletal", "neurological", "nutritional and metabolic", "ocular and sensory", "renal", "reproductive", "respiratory", and "skin and connective tissue". The details of these health outcome search strategies that underlie the filters are available online. Studies that included one or more of the search terms in the title, abstract, keyword, or MeSH fields were exported and used to populate the Hazard Heat Map (Figure 2-10). Studies that were not retrieved using these filters were tagged as "No Tag". The evidence type listed in the heat map (*e.g.*, human, animal-human health model, animal-environmental model, and plant) was manually assigned to each reference by screeners during the full-text screening.

The health outcome tags were originally designed for vertebrate systems, and as such, did not conform well to plant evidence. Therefore, any plant studies tagged for: "cancer", "cardiovascular", "gastrointestinal", "hematological and immune", "hepatic", "musculoskeletal", "neurological", "ocular and sensory" and "renal and respiratory" were manually reviewed and re-tagged to more appropriate health outcomes.

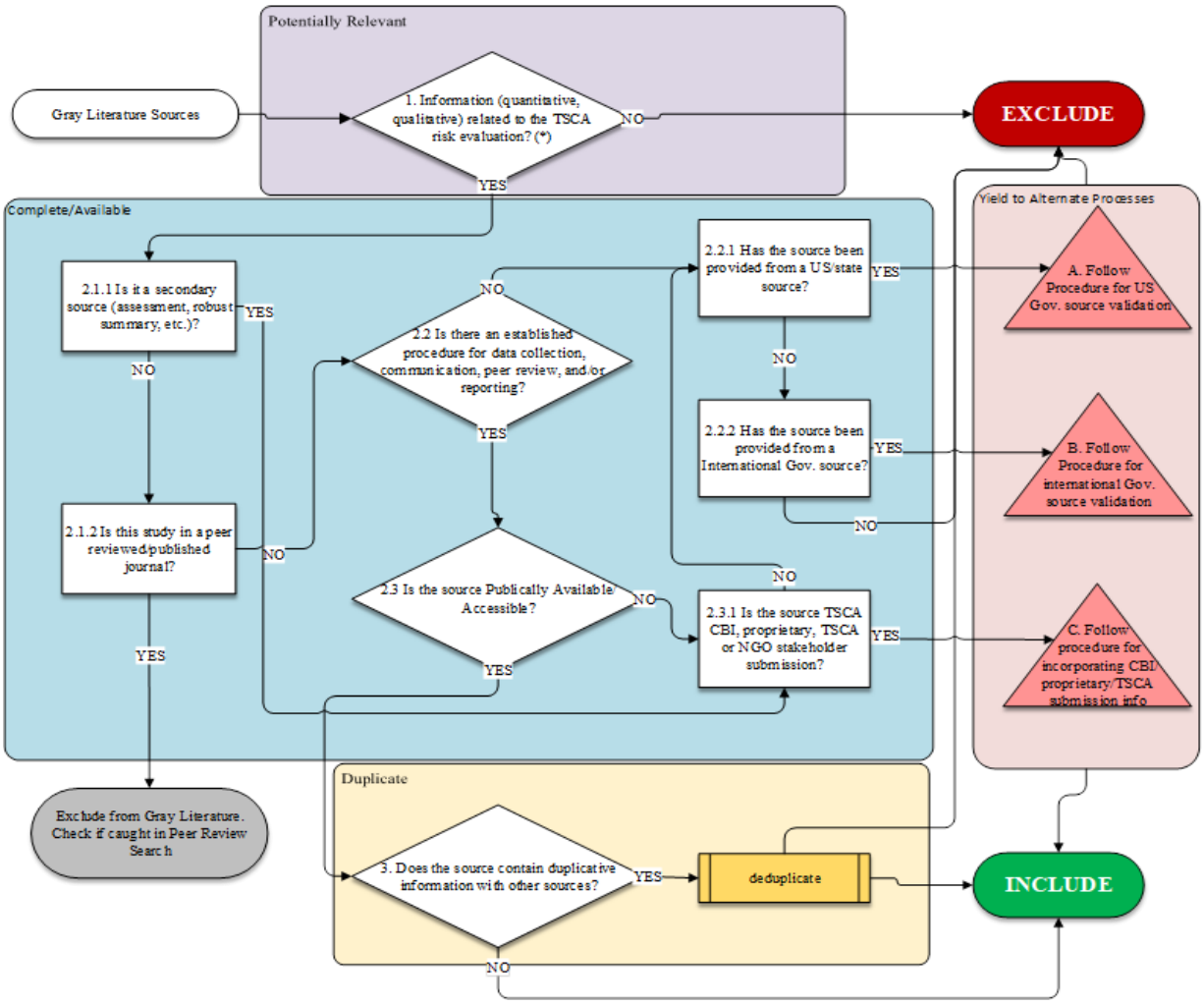
A.3 Gray Literature Search and Screening Strategies

EPA conducted a gray literature search for reasonably available information to support the manufacturer requested TSCA risk evaluation for D4. Gray literature is defined as the broad category of data/information sources not found in standard, peer-reviewed literature databases (*e.g.*, PubMed and Web of Science). Gray literature includes data/information sources such as white papers, conference proceedings, technical reports, reference books, dissertations, information on various stakeholder websites, and other databases. Given the nature of how gray literature is searched and collected, results may not come with a bibliographic citation or abstract and were therefore processed using a decision tree logic described in Appendix A.3.1 for potential relevance prior to entering full-text screening where a discipline-specific PECO is applied.

Search terms were variable dependent on source and based on knowledge of a given source to provide discipline-specific information. A summary of sources is provided in Appendix A.3.4. The criteria for determining the potential relevance of documents identified from gray literature sources is described in the following sections for each discipline.

A.3.1 Screening of Gray Literature

To reduce the overall burden of processing gray literature results, EPA developed a screening process to determine the potential relevance of gray literature. This step was introduced prior to collecting the resulting documents. Figure_Apx A-1 describes the decision logic used to screen gray literature results.



Figure_Apx A-1. Decision Logic Tree Used to Screen Gray Literature Results

A.3.2 Initial Screening of Sources using Decision Logic Tree

The purpose of the inclusion/exclusion decision logic tree in Figure_Apx A-1 is to provide a broad, general screening technique to determine whether each gray literature source should be included and further screened or excluded with no additional screening necessary. The diamonds in the decision tree require analysis by the screener, whereas the rectangular boxes are used to classify the type of source. All the questions used in the decision process are provided in Table_Apx A-12**.**

Table_Apx A-12. Decision Logic Tree Overview

Step	Metric	Questions to Consider
1	Potential Relevance	Does the result have information (qualitative or quantitative) related to TSCA risk evaluations?[a]
2.1.1	Complete / Available	Is it a secondary data source (assessment, robust summary, TSCA submission databases, etc.)?
2.1.2		Is the document from a peer-reviewed/published journal?

Step	Metric	Questions to Consider
2.2		Is there an established procedure for data collection, communication, peer review, and/or reporting?
2.2.1		Has the data been provided by a US governmental/state source?
2.2.2		Has the data been provided by an international governmental source?
2.3		Are these data publicly available/accessible?
2.3.1		Is the source TSCA CBI, proprietary, TSCA or NGO stakeholder submission?
3	Duplicate	Does the result contain any duplicative information found in other sources?
[a] Apply discipline relevancy metric		

Results of the gray literature search and decision tree process are included in Appendix A.3.3.

A.3.3 TSCA Submission Searching and Title Screening

EPA screens information submitted under TSCA sections 4, 5, 8(e), and 8(d), as well as for your information (FYI) submissions. In the gray literature process defined in Appendix A.3.2, EPA considers the databases that contain TSCA submissions to be secondary sources (Step 1.1) because the metadata in the databases are secondary. These databases then advance to Step 2.3.1 and then to Process C. The Process C steps are described here.

EPA first screens the titles using two screeners per title. EPA conducts this step primarily to reduce the number of full studies to be obtained because some studies are available only on microfiche or in long-term storage. Screening is done using the inclusion and exclusion criteria within the relevant PECOs, PESOs or RESOs for each topic area (Appendix A.2.1). EPA excludes interim reports (*e.g.*, interim sacrifices for toxicity studies) and only final reports are further considered. If the title is not clear regarding the document's contents, EPA obtains the full-text and advances to the next steps.

After full texts are obtained, EPA reviews some sources (prior to full-text screening) based on whether they have several factors; primary data, an established procedure for peer review, data collection, communication and/or reporting and are publicly available. Sources that have these factors will move on to full-text screening. Other sources will go straight to full-text screening using PECO-type criteria without going through this extra step.

EPA may decide to initiate a backwards search on sources that are deemed to have secondary data. In situations where parameters such as procedures for peer review and data collection are unclear, EPA may reach out to the authors to retrieve information to gauge whether the source should be included or excluded. Studies that are not publicly available (such as proprietary or CBI sources) may undergo additional screening steps.

During the full-text screening step, two individuals screen each source according to the PECOs, PESOs and RESOs (Appendix A.2.1).

Results of the TSCA submission search and decision tree process are included in Appendix A.3.4

A.3.4 Gray Literature Search Results for D4

Table_Apx A-13 provides a list of gray literature sources that yielded results for D4.

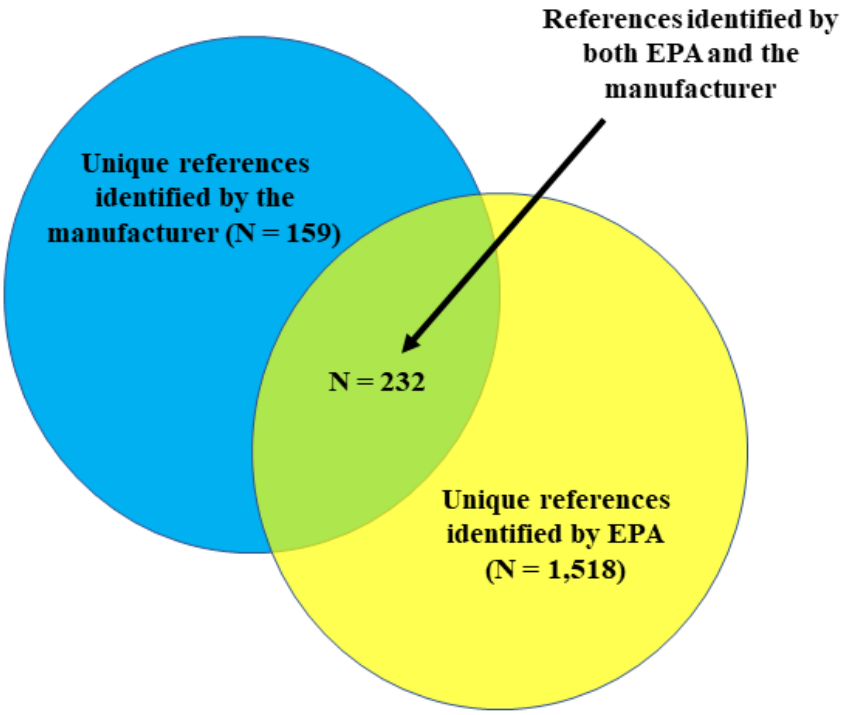
Table_Apx A-13. Gray Literature Sources that Yielded Results for D4

Source Agency	Source Name	Source Type	Source Category	Source Website
OECD	OECD: Emission Scenario Documents	International Resources	Assessment or Related Document	http://www.oecd.org/document/46/0,2340,en_2649_201185_2412462_1_1_1_1,00.html
OECD	OECD: General Site	International Resources	General Search	https://www.oecd.org/
Env Canada	Priority Substances List Assessment Report; State of Science Report, Environment Canada Assessment	International Resources	Assessment or Related Document	https://www.canada.ca/en/environment-climate-change/services/canadian-environmental-protection-act-registry/substances-list/priority-list.html
Env Canada	Screening Assessment for the Challenge	International Resources	Assessment or Related Document	https://www.canada.ca/en/health-canada/services/chemical-substances/challenge/list.html
Aus. Assm.	NICNAS Assessments (Eco)	International Resources	Assessment or Related Document	https://www.nicnas.gov.au/chemical-information/imap-assessments/imap-assessments
Aus. Assm.	NICNAS Assessments (Human Health, Tier I, II or III)	International Resources	Assessment or Related Document	https://www.nicnas.gov.au/chemical-information/imap-assessments/imap-assessments
CPSC	Technical Reports: Exposure/Risk Assessment	Other US Agency Resources	Technical Report	https://www.cpsc.gov/Research--Statistics/Chemicals
NLM	National Library of Medicine's HazMap	Other US Agency Resources	Database	https://haz-map.com/

Source Agency	Source Name	Source Type	Source Category	Source Website
NLM	National Library of Medicine's PubChem	Other US Agency Resources	Database	https://pubchem.ncbi.nlm.nih.gov/
EPA	Office of Air: Air Emission Factors (AP-42)	US EPA Resources	Regulatory Document or List	https://www.epa.gov/air-emissions-factors-and-quantification/ap-42-compilation-air-emissions-factors
EPA	EPA Office of Water: Ambient Water Quality Criteria documents	US EPA Resources	Assessment or Related Document	https://www.epa.gov/wqc
EPA	EPA: Generic Scenario	US EPA Resources	Assessment or Related Document	https://www.epa.gov/tsca-screening-tools/chemsteer-chemical-screening-tool-exposures-and-environmental-releases#genericscenarios
ECHA	European Chemicals Agency (ECHA) Documents	International Resources	Assessment or Related Document	https://echa.europa.eu/information-on-chemicals
TERA	International Toxicity Estimates for Risk (ITER)	Other Resources	Database	https://tera.org/iter/
KOECT	Kirk-Othmer Encyclopedia of Chemical Technology Journal Article	Other Resources	Encyclopedia	https://onlinelibrary.wiley.com/doi/book/10.1002/0471238961

A.4 Summary of Literature Cited in the SEHSC Submission

As part of the SEHSC submission requesting the risk evaluation for D4 (Docket ID: EPA-HQ-OPPT-2018-0443), data were submitted to EPA separately from the systematic review search process outlined for peer-reviewed and gray literature data in Appendix A.2 and Appendix A.3, respectively. Data from the SEHSC submission were compared to the search results from the systematic review process to determine the overlap in the reference pools. The manufacturer submitted 391 total references with their request. In the separate systematic review search process, EPA identified 1,750 total references, 232 of which had already been provided by the manufacturer and 1,518 of which were not included in the SEHSC submission (as shown in Figure_Apx A-2). The remaining 159 sources provided by the manufacturer that were not captured in the peer-review and TSCA search submissions for D4 data will undergo the appropriate systematic review steps (*e.g.*, additional deduplication, full-text screening, data evaluation and integration). Therefore, EPA may refine and revise the numbers in Figure_Apx A-2 following further evaluation using systematic review methods.



Figure_Apx A-2. Venn Diagram of Literature Identified by EPA vs. the SEHSC Submission

Appendix B PHYSICAL AND CHEMICAL PROPERTIES OF D4

Table_Apx B-1 summarizes statistics for the physical and chemical property values identified through systematic review as of January 2021. The "N" column indicates the number of unique primary sources of data for that endpoint. That is, if multiple sources presented equivalent values and cited the same primary source, only one of those was included in these statistics and included in the statistical calculations. All physical and chemical property values that were extracted and evaluated as of January 2021 are presented in the supplemental file *Data Extraction and Data Evaluation Tables for Physical and Chemical Property Studies* (Docket ID: EPA-HQ-OPPT-2018-0443).

Table_Apx B-1. Physical and Chemical Properties of D4

Property or Endpoint	N	Unit	Mean	Standard Deviation	Min	Max
Molecular formula	–	–	NA	NA	NA	NA
Molecular weight	–	g/mol	NA	NA	NA	NA
Physical state	3	–	NA	NA	NA	NA
Physical properties	5	–	NA	NA	NA	NA
Melting point	20	°C	17.6	1.5	170.0	18.5
Boiling point	16	°C	175.2	1.5	170.0	176.4
Density	11	g/cm^3	0.956	0.002	0.9497	0.9600
Vapor pressure	5	mm Hg	0.946	0.148	0.696	1.05
Vapor density	0	–	–	–	–	–
Water solubility	2	mg/L	0.065	0.013	0.056	0.074
Octanol/water partition coefficient (log Kow)	2	–	6.95	0.04	6.92	6.98
Henry's Law constant	4	$atm \cdot m^3/mol$	5.05	5.77	0.08	11.8
Flash point	6	°C	55.7	1.0	54.0	57.0
Auto flammability	0	°C	–	–	–	–
Viscosity	5	cP	2.375	0.207	2.187	2.700
Refractive index	8	–	1.3967	0.0022	1.394	1.401
Dielectric constant	1	–	–	–	–	–
NA = Not applicable						

Appendix C ENVIRONMENTAL FATE AND TRANSPORT PROPERTIES OF D4

Table_Apx C-1 provides the environmental fate characteristics that EPA identified and considered in developing the scope for D4. This table may be updated as EPA collects additional information through systematic review methods and by reviewing information provided in the SEHSC submission requesting the risk evaluation for D4 (Docket ID: EPA-HQ-OPPT-2018-0443).

Table_Apx C-1. Environmental Fate and Transport Properties of D4

Property or Endpoint	Value[a]	Reference
Direct photodegradation	Not expected to be susceptible to direct photolysis by sunlight because D4 does not contain chromophores that absorb at wavelengths >290 nm	NLM (2020)
Indirect photodegradation	$t_{1/2}$ > 2,500 years (based O_3 of 10^{-9} mol/L in urban locations)	Brooke et al. (2009) based on Abe et al. (1981)
Indirect photodegradation	$t_{1/2}$ = 11.4 days (based on •OH reaction rate constant of 0.94×10^{-12} cm^3/mol·second at 24 ºC and a 12-hour day with 1×10^6 OH/cm^3)	Atkinson (1991)
	$t_{1/2}$ = 8.5 days (based on •OH reaction rate constant of 1.3×10^{-12} cm^3/mol·second at 24 ºC and a 12-hour day with 1.5×10^6 OH/cm^3)	Sommerlade et al. (1993)
	$t_{1/2}$ = 5.1 days (based on •OH reaction rate constant of 2.1×10^{-12} cm3/mol·second at 40 ºC and a 12-hour day with 1.5×10^6 OH/cm^3)	Safron et al. (2015)
	$t_{1/2}$ = 4.7 days (based on •OH reaction rate constant of 2.3×10^{-12} cm3/mol·second at 40 ºC and a 12-hour day with 1.5×10^6 OH/cm^3)	Xiao et al. (2015)
	$t_{1/2}$ = 11.3 days (based on •OH reaction rate constant of 0.95×10^{-12} cm3/mol·second at 25 ºC and a 12-hour day with 1.5×10^6 OH/cm^3)	Kim and Xu (2017)
	$t_{1/2}$ = 10.1 days (based on •OH reaction rate constant of 1.1×10^{-12} cm3/mol·second at 21 ºC and a 12-hour day with 1.5×10^6 OH/cm^3)	Bernard et al. (2018)
	$t_{1/2}$ = 2.2 days calculated from measured atmospheric D4 concentrations (excluding	Xu et al. (2019b)

Property or Endpoint	Value[a]	Reference
	manufacture sites, wastewater treatment plants, and landfills)	
	$t_{1/2}$ = 8.3 days (based on •OH reaction rate constant of 1.3×10^{-12} cm^3/mol·second at 24 ºC and a 12-hour day with 1.5×10^6 OH/cm^3)	Alton and Browne (2020)
Hydrolysis (water)	$t_{1/2}$ = 21 days at pH 7 and 10 ºC into linear siloxanes with dimethylsilanediol (DMSD) as final product (OECD 111)	EC/HC (2008) based on Durham (2005)
	$t_{1/2}$ = 16.7 days at pH 7 and 12 ºC; $t_{1/2}$ = = 2.9 days at pH 8 and 9 ºC into linear siloxanes with dimethylsilanediol (DMSD) as final product (OECD 111)	Brooke et al. (2009) based on Durham (2005)
	$t_{1/2}$ = 15.2, 4.1, 1.6, and 0.4 days at 4, 20, 35, and 55 ºC (respectively) and pH 7 (OECD 111)	Gatidou et al. (2016)
	$t_{1/2}$ = 15.6, 6.3, and 2.3 hours at pH 7.8, 8.5, and 9.2 (respectively) and 22 ºC with dimethylsilanediol (DMSD) as final product	Xu et al. (2016)
Hydrolysis (sediment)	$t_{1/2}$ = 49 days 22 to 25 ºC into linear siloxanes with dimethylsilanediol (DMSD) as final product (OECD 308)	EC/HC (2008) based on Xu and Miller (2008)
	$t_{1/2}$ = 365 days in anaerobic sediment and 242 days in aerobic sediment at 24 ºC (OECD 308)	ECHA (2015a) based on Xu (2009) and Xu and Miller (2009)
Abiotic degradation in soil	$t_{1/2}$ = 1 to 22 hours in Oxisol from Hawaii $t_{1/2}$ = 3.5 to 22 days in Alfisol from Michigan Rate depends on soil water content with dimethylsilanediol (DMSD) as final product	Xu (1999) and Xu and Chandra (1999)
	$t_{1/2}$ = 3.3, 3.4, 6.2, 7.9, and 11.6 hours in soil with 20.7% clay and with crude oil at 0.08, 0.4, 2, 10, and 40 mg/g (respectively) at 25 ºC (capped vials)	Shi et al. (2015)

Property or Endpoint	Value[a]	Reference
	$t_{1/2}$ = 5.6, 7.4, 8.8, 15.1, and 21.1 days in soil with 20.7% clay and with crude oil at 10, 20, 50, 100, and 200 mg/g (respectively) at 25 ºC	Xu et al. (2019a)
	$t_{1/2}$ = 4.1 to 5.3 days in temperate soil at relative humidity of 50 to 90%	SEHSC (2020) based on Xu (2007)
Biodegradation (aerobic)	Not likely to undergo biodegradation in water based on limited biodegradation (3.7%) in 28 days (OECD 310)	EC/HC (2008) based on Gledhill (2005)
Biodegradation (anaerobic)	Not likely to undergo anaerobic biodegradation based on limited biodegradation (3%) after 100 days under anaerobic conditions with sewage sludge	Grümping et al. (1999)
Wastewater treatment	89% mean total removal from four wastewater treatment facilities	HydroQual Inc (1993)
	94.6% average total removal (57 to 60% by sludge and 33 to 38% by volatilization) at three wastewater treatment facilities	Mueller et al. (1995)
Wastewater treatment	86.4% total removal at pilot plant system	Parker et al. (1999)
	5% total removal (9% by sludge) at one wastewater treatment facility	Bletsou et al. (2013)
	76 to 93% average total removal (19 to 29.4% by excess sludge) by traditional process and 59% by reverse osmosis from measurements at three wastewater treatment facilities	Xu et al. (2013)
	98% mean total removal at 11 wastewater treatment facilities	Wang et al. (2013b)
	96% total removal (29% by sludge) at one wastewater treatment facility	Wang et al. (2015)
	100% total removal by biological aerated filter and (35% by sludge) and 85.7% total removal by anaerobic-oxic (65% by sludge) at two wastewater treatment facilities	Li et al. (2016)

Property or Endpoint	Value[a]	Reference
	76% total removal (27% by sludge) at one wastewater treatment facility	Xu et al. (2016)
	96% mean total removal at nine wastewater treatment facilities	Horii et al. (2019)
	99% total removal (0% by biodegradation, 60% by sludge, 39% by volatilization to air; estimated)[b]	U.S. EPA (2012b)
Bioconcentration factor (Log BCF)	4.09 (BCFss = 12,400 L/kg) in fathead minnows (*Pimephales promelas*) using radio-labelled D4	Fackler et al. (1995)
	3.48 to 3.74 (BCFss = 3,000 to 4,000 and BCFk = 4,100 to 5,500) common carp (*Cyprinus carpio*)	ECHA (2015b)
	3.47 (BCF_k = 2,953 L/kg wet weight) calculated for rainbow trout (*Oncorhynchs mykiss*) using a model accounting for adsorption, distribution, metabolism, elimination	SEHSC (2020)
	3.32 (BCF = 2,104 L/kg wet weight) in common carp (*Cyprinus carpio*) based on rates of update and clearance	Xue et al. (2020)
	4.11 (BCF = 1.30×10^4) (estimated)[b]	U.S. EPA (2012b)
Bioaccumulation factor (Log BAF)	4.11 (BCF = 1.30×10^4) (estimated)[b]	U.S. EPA (2012b)
Biomagnification factor (BMF) (kg lipid/kg lipid unless noted)	0.18 to 4.6 for rainbow trout (*Oncorhynchs mykiss*)	Brooke et al. (2009)
	2.4 for lake trout (*Salvelinus namaycush*)-small yellow perch (*Perca flavescens*) and 1.9 for lake trout-small cisco (*Coreogonus artedi*) predator-prey relationships at Lake Opeongo, Canada	ECHA (2012) based on Dow Corning (2010)
	1.0 to 1.4 for Atlantic cod (*Gadus morhua*)-Northern shrimp (*Pandalus borealis*) and 1.0 for Atlantic cod-Atlantic herring (*Clupea harengus*) predator-prey relationships at Inner and Outer Oslofjord, Norway	ECHA (2012) based on Dow Corning (2010)
	0.66 (concentration of food/fish) and 4.0 (rate of uptake/clearance) for	Woodburn et al. (2013)

Property or Endpoint	Value[a]	Reference
	rainbow trout (*Oncorhynchs mykiss*) (OECD 305)	
	0.51 and 0.7 growth normalized for common carp (*Cyprinus carpio*) (OECD 305)	ECHA (2015b)
	3.2 for Japanese snapping shrimp (*Alpheus japonicus*)-planktons based on stable isotope analysis	Xue et al. (2019)
	0.36 calculated for rainbow trout (*Oncorhynchs mykiss*) using a model accounting for adsorption, distribution, metabolism, elimination	SEHSC (2020)
Biota sediment accumulation factor (BSAF)	13.3 to 20 for oligochaete (*Lumbriculus variegatus*) from sediment spiked with D4	(ECHA, 2012) based on Wildlife International Ltd (2008)
Biota sediment accumulation factor (BSAF)	2.2, 1.3, and 0.7 for midge (*Chironomus tentans*) larvae in sediment with 0.3, 2.3, and 4.1 organic carbon content (%), respectively	Wang et al. (2013a) based on Kent et al. (1994)
	>1 for many species (especially for some benthic invertebrate species) in a freshwater lake	Wang et al. (2013a) based on Powell et al. (2009)
	0.445 to 1.61 in bottom fish (*Hexagrammos otakii*) from the marine sea near Dalian, China	Hong et al. (2014)
	≤6.2 in Artic char (*Salvelinus alpinus*) and from 0.5 to 3.3 in three-spined sticklebacks (*Gasterosteus aculeatus*) from Lake Storvannet, Norway	Krogseth et al. (2017)
	0.42 in mollusks including mussel (*Mytilus galloprovincialis*), venus clam (*Cyclina sinensis*), and oyster (*Crassostrea talienwhanensis*) from Bohai Sea, China	Zhi et al. (2019)
Trophic magnification factor (TMF) (kg lipid/kg lipid unless noted)	0.24 to 0.36 freshwater aquatic food chain in Lake Pepin, Minnesota	ECHA (2012) based on Powell et al. (2009)
	D4 was below the level of quantitation in most of samples from	Borgå et al. (2013)

Property or Endpoint	Value[a]	Reference
	pelagic freshwater food web of Lakes Mjøsa and Randsfjorden, Norway	
	0.73 to 1.1 in food web of Lake Erie	McGoldrick et al. (2014)
	1.16 in food web of the Dalian Bay, Chinese Yellow Sea, China	Jia et al. (2015)
	1.3 (least squares regression) and 0.6 (bootstrap) in food web of Tokyo Bay, Japan	Powell et al. (2017)
	0.5 to 0.7 in food web of Inner and Outer Oslofjord, Norway	Powell et al. (2018)
	1.7 in food web of Bohai Sea, China	Cui et al. (2019)
	No significant relationship with trophic position in food web of Inner Oslofjord, Norway	Norwegian Environment Agency (2019)
	<1 in food web of Shuangtaizi estuary, China	Xue et al. (2019)
Soil organic carbon:water partition coefficient (Log Koc)	4.22 (K_{OC} = 1.66×10^4)	Kozerski et al. (2014)
	6.27 (K_{OC} = 184.3×10^4) at 0 ºC (Calculated) 5.99 (K_{OC} = 98.4×10^4) at 5 ºC (Calculated) 5.06 (K_{OC} = 11.5×10^4) at 21 ºC 5.17 (K_{OC} = 14.8×10^4) at 25 ºC	Panagopoulos et al. (2017)
	4.21 (K_{OC} = 1.62×10^4; MCI method); 4.35 (K_{OC} = 2.26×10^4; K_{ow} method) (estimated)[b]	U.S. EPA (2012b)
Dissolved organic carbon:water partition coefficient (Log K_{DOC})	5.05 (K_{DOC} = 11.2×10^4)	Panagopoulos et al. (2015)
Sludge:water partitioning coefficient (KogK_d)	1.94 to 4.05 (K_d = 88 to 11350 L/kg) at two wastewater treatment facilities	Xu et al. (2013)
	3.38 (K_d = 2,399 L/kg) mean value at one wastewater treatment facility	Bletsou et al. (2013)
	3.30 (K_d = 1,995 L/kg) to primary sludge and 3.64 (Kd = 4,365 L/kg) to secondary sludge	Wang et al. (2015)

Property or Endpoint	Value[a]	Reference
	2.32 (K_d = 209 L/kg) to anaerobically digested sludge at 35 ºC	Gatidou et al. (2016)

[a] Measured unless otherwise noted.

[b] EPI Suite Physical Property Inputs: Log Kow = 6.74; MP = 17.5 ºC; VP = 1.05 mm Hg; WS = 0.056 mg/L); SMILES C[Si]1(C)O[Si](C)(C)O[Si](C)(C)O[Si](C)(C)O1

Appendix D REGULATORY HISTORY

The chemical substance, D4, is subject to federal and state laws and regulations in the United States (Table_Apx D-1 and Table_Apx D-2). Regulatory actions by other governments, tribes, and international agreements applicable to D4 are listed in Table_Apx D-3.

D.1 Federal Laws and Regulations

Table_Apx D-1. Federal Laws and Regulations

Statutes/Regulations	Description of Authority/Regulation	Description of Regulation
EPA statutes/regulations		
Toxic Substances Control Act (TSCA) – section 8(a)	The TSCA section 8(a) CDR Rule requires manufacturers (including importers) to give EPA basic exposure-related information on the types, quantities and uses of chemical substances produced domestically and imported into the United States.	D4 manufacturing (including importing), processing, and use information is reported under the CDR rule (85 FR 20122, April 9, 2020).
Toxic Substances Control Act (TSCA) – section 8(b)	EPA must compile, keep current and publish a list (the TSCA Inventory) of each chemical substance manufactured (included imported) or processed in the United States.	D4 (Cyclotetrasiloxane, 2,2,4,4,6,6,8,8-octamethyl-) was on the initial TSCA Inventory and therefore was not subject to EPA's new chemicals review process under TSCA section 5 (60 FR 16309, March 29, 1995)
Toxic Substances Control Act (TSCA) – section 8(d)	Provides EPA with authority to issue rules requiring producers, importers, and (if specified) processors of a chemical substance or mixture to submit lists and/or copies of ongoing and completed, unpublished health and safety studies.	Two substantial risk reports received for D4: one 1996 reproductive toxicity report, one 2017 environmental monitoring report. (U.S. EPA, ChemView. Accessed December 16, 2020).
Toxic Substances Control Act (TSCA) – section 8(e)	Manufacturers (including importers), processors, and distributors must immediately notify EPA if they obtain information that supports the conclusion that a chemical substance or mixture presents a substantial risk of injury to health or the environment.	Thirty-nine risk reports were received for D4 (Received: 1992-2017). U.S. EPA, ChemView. (Accessed December 16, 2020).
Toxic Substances Control Act (TSCA) – section 4	Provides EPA with authority to issue rules, enforceable consent agreements and orders requiring manufacturers (including importers) and processors to test chemical substances and mixtures.	EPA required testing for the presence of D4 in several environmental media under an enforceable consent agreement with five manufacturers. The testing was completed in 2017

Statutes/Regulations	Description of Authority/Regulation	Description of Regulation
		and the final test report can be found in docket EPA-HQ-OPPT-2012-0209. Thirteen chemical data submissions from test rules received for D4: one acute aquatic plant toxicity study, four acute aquatic toxicity studies, three chronic aquatic toxicity studies, two bioaccumulation potential studies and two water solubility studies. (U.S. EPA, ChemView. Accessed December 16, 2020).
Other federal statutes/regulations		
Federal Food, Drug, and Cosmetic Act (FFDCA) –section 408	FFDCA governs the allowable residues of pesticides in food. section 408 of the FFDCA provides EPA with the authority to set tolerances (rules that establish maximum allowable residue limits), or exemptions from the requirement of a tolerance, for pesticide residues (including inert ingredients) on food. Prior to issuing a tolerance or exemption from tolerance, EPA must determine that the pesticide residues permitted under the action are "safe." section 408(b) of the FFDCA defines "safe" to mean a reasonable certainty that no harm will result from aggregate, nonoccupational exposures to the pesticide. Pesticide tolerances or exemptions from tolerance that do not meet the FFDCA safety standard are subject to revocation under FFDCA section 408(d) or (e). In the absence of a tolerance or an exemption from tolerance, a food containing a pesticide residue is considered adulterated and may not be distributed in interstate commerce.	D4 (Cyclotetrasiloxane, octamethyl-) is approved for nonfood use. D4 (Methylated silicones) is approved for food use as an antifoaming agent used pre- and post-harvest. CFR 180.910, reassessed 6/1/2006 (Accessed December 16, 2020)

D.2 State Laws and Regulations

Table_Apx D-2. State Laws and Regulations

State Actions	Description of Action
Chemicals of High Concern to Children	Several states have adopted reporting laws for chemicals in children's products containing D4, including Vermont (18 V.S.A § 1776), Maine[10] (38 MRSA Chapter 16-D), and Minnesota (Toxic Free Kids Act Minn. Stat. 116.9401 to 116.9407). Two states have amended their reporting laws for chemicals in children's products containing D4, including Oregon (no longer needs to be reported as of January 1, 2019) (Oregon Toxic-Free Kids Act, Senate Bill 478, 2015) and Washington State (CHCC removed by Rule Amendment in 2017) (Wash. Admin. Code 173-334-130).
Other	California lists D4 as a designated priority chemical for biomonitoring under criteria established by California SB 1379 (Biomonitoring California, Priority Chemicals, February 2019). The Oregon Department of Environmental Quality lists D4 as a priority persistent pollutant (Oregon SB 737). New York proposed Bill No A06892 to Amend the General Business Law, in Relation to Requiring Cosmetic Packaging to Bear a Warning Label, would require warning labels on cosmetics containing D4 (A. 6892, 232nd Leg., Reg. Sess. (N.Y. 2009)).

D.3 International Laws and Regulations

Table_Apx D-3. Regulatory Actions by Other Governments, Tribes, and International Agreements

Country/ Organization	Requirements and Restrictions
Canada	D4 is on the Domestic Substances List. (Government of Canada. Managing substances in the environment. Substances search. Accessed December 15, 2020). D4 is on the is on the Canadian List of Toxic Substances (CEPA 1999 Schedule 1). Canada required pollution prevention plan implementation

[10] Maine added D4 to its reporting laws for chemicals in children's products in July 2009 (38 MRSA Chapter 16-D). In January 2017, Maine DEP received a petition to remove certain silicone substances from the Chemicals of Concern list. D4 was not included in that request (https://www.maine.gov/dep/safechem/childrens-products/concern/documents/Maine-Siloxane-petition-determination.pdf).

Country/ Organization	Requirements and Restrictions
	for D4 in 2017 for industrial effluents to prevent or minimize D4 releases to the environment from industrial users (Canada Gazette, Part I, Saturday, January 15, 2011; Vol. 145, No. 3, Supplement). The Government of Canada published a Draft Screening Assessment for the Siloxanes Group on June 1, 2019. (https://www.canada.ca/en/environment-climate-change/services/evaluating-existing-substances/draft-screening-assessment-siloxanes-group.html)
European Union	D4 is registered for use in the EU. (European Chemicals Agency (ECHA) database. Accessed December 15, 2020. In 2018, D4 was added Annex XVII of regulation (EC) No 1907/2006 - REACH (Registration, Evaluation, Authorization and Restriction of Chemicals). The restriction stipulates that D4 shall not be placed on the market in wash-off cosmetic products in a concentration equal to or greater than 0.1 % by weight after January 31, 2020. (ECHA database. Accessed December 16, 2020).[11] In 2018, D4 was listed on the Candidate list as a Substance of Very High Concern (SVHC) under regulation (EC) No 1907/2006 - REACH due to meeting the criteria for identification as a PBT (Article 57d) and vPvB substance (Article 57e). (ECHA database. Accessed December 15, 2020).[12] In 2019 an intent to register a restriction proposal was submitted. The restriction would stipulate that leave-on personal care products and other consumer/professional products containing D4 in concentrations > 0.1% shall not be placed on the market. (ECHA database. Accessed December 15, 2020).
Australia	D4 was assessed under Environmental Tier II of the Inventory Multi-Tiered Assessment and Prioritisation (IMAP). (National Industrial Chemicals Notification and Assessment Scheme (NICNAS). Chemical inventory. Database accessed December 15, 2020).
Japan	D4 is regulated in Japan under the Act on the Evaluation of Chemical Substances and Regulation of Their Manufacture, etc. (Chemical

[11] In April 2018, industry filed a legal action in the Court of Justice of the European Union (General Court) seeking, among other things, annulment of the Wash-Off Restriction. See https://eurlex.europa.eu/legal-content/EN/TXT/?qid=1570630612867&uri=CELEX:62018TN0226.

[12] In September 2018, industry filed a legal action in the Court of Justice of the European Union (General Court) seeking annulment of the ECHA decision to list D4 as a SVHC. See https://eurlex.europa.eu/legal-content/EN/TXT/?qid=1518304338301&uri=CELEX:62018TN0519.

Country/ Organization	Requirements and Restrictions
	Substances Control Law; CSCL) (National Institute of Technology and Evaluation [NITE] Chemical Risk Information Platform [CHIRP]. Accessed December 15, 2020).
United Kingdom	D4 was assessed based on the methods outlined in the European Union (EU) Technical Guidance Document (TGD) for the risk assessment of new and existing chemicals (Environmental Risk Assessment Report for Octamethylcyclotetrasiloxane). (UK Environment Agency. April 2019)

Appendix E PROCESS, RELEASE, AND OCCUPATIONAL EXPOSURE INFORMATION

This appendix provides information and data found in preliminary data gathering for D4.

E.1 Process Information

Process-related information potentially relevant to the risk evaluation may include process diagrams, descriptions, and equipment. Such information may inform potential release sources and worker exposure activities.

E.1.1 Manufacture (Including Import)

In the 2016 CDR, 9 facilities reported manufacturing or importing D4 for calendar year 2015. According to the 2016 public CDR data, D4 is manufactured as a liquid, and may be imported as either a liquid or a dry powder (U.S. EPA, 2020a).

E.1.1.1 Domestic Manufacturing

The manufacture of siloxane compounds involves a series of reactions. First, the starting material, quartz (silica), is mixed with coke and reduced to silicon metal by heating in an electric arc furnace. The silicon metal then reacts with methyl chloride vapor to produce chlorosilanes. Subsequent hydrolysis of chlorosilanes and condensation of silanol intermediate then produce a mixture of linear and cyclic siloxanes, which can be further processed, split, or distilled into specific siloxane compounds such as D4 (EPA-HQ-OPPT-2018-0443-0004).

E.1.1.2 Import

Commodity chemicals such as D4 may be imported into the United States in bulk via water, air, land, and intermodal shipments (Tomer and Kane, 2015). These shipments take the form of oceangoing chemical tankers, railcars, tank trucks, and intermodal tank containers. Chemicals shipped in bulk containers may be repackaged into smaller containers for resale, such as drums or bottles. Domestically manufactured commodity chemicals may be shipped within the United States in liquid cargo barges, railcars, tank trucks, tank containers, intermediate bulk containers (IBCs)/totes, and drums. Both imported and domestically manufactured commodity chemicals may be repackaged by wholesalers for resale; for example, repackaging bulk packaging into drums or bottles. The type and size of container will vary depending on customer requirement. In some cases, QC samples may be taken at import and repackaging sites for analyses. Some import facilities may only serve as storage and distribution locations, and repackaging/sampling may not occur at all import facilities.

According to the 2016 CDR, D4 may be imported as a neat liquid (greater than 90 percent concentration by weight), or as part of a liquid or dry powder formulation containing 1 to 30 percent D4 by weight. (U.S. EPA, 2020a).

E.1.2 Processing and Distribution

E.1.2.1 Reactant or Intermediate

Processing as a reactant or intermediate is the use of D4 as a feedstock in the production of another chemical via a chemical reaction in which D4 is consumed to form the product. A major use of D4 is as a monomer for silicone polymers. In this process, D4 undergoes equilibration polymerization to make polydimethylsiloxane (PDMS) and a wide range of functionalized siloxanes bearing.

D4 is also an intermediate to produce decamethyltetrasiloxane. In this process, D4 and hexamethyldisiloxane are fed to a reactor and allowed to reach equilibrium. The equilibrate is removed from the reactor and distilled to separate the desired product from the unreacted hexamethyldisiloxane and D4, which are returned to the reactor (EPA-HQ-OPPT-2018-0443-0004).

E.1.2.2 Incorporated into a Formulation, Mixture, or Reaction Product

Incorporation into a formulation, mixture or reaction product refers to the process of mixing or blending of several raw materials to obtain a single product or preparation. Exact process operations involved in the incorporation of D4 into a chemical formulation, mixture, or reaction product are dependent on the specific manufacturing process or processes involved. According to the 2016 CDR and the SEHSC submission (EPA-HQ-OPPT-2018-0443-0004), D4 is used as an intermediate in synthetic rubber manufacturing, cyclic crude and intermediate manufacturing, and all other basic inorganic chemical manufacturing. D4 and polymer containing residual D4 monomer can also be processed and incorporated into various end products in many industrial sectors including computer and electronic product manufacturing, asphalt paving, roofing, and coating materials manufacturing, electrical equipment, appliance, and component manufacturing, rubber product manufacturing, and all other chemical product and preparation manufacturing and miscellaneous manufacturing (U.S. EPA, 2020a) and (EPA-HQ-OPPT-2018-0443-0004).

E.1.2.3 Repackaging

Repackaging refers to preparation of a chemical substance for distribution into commerce in a different form, state, or quantity than originally received/stored, where such activities include transferring a chemical substance from a bulk storage container into smaller containers.

E.1.3 Uses

E.1.3.1 Adhesives and Sealants

D4 may be present in a number of adhesive and silicone sealants at concentrations ranging from less than one percent to up to 10 percent. Adhesive application method depends on a variety of factors including the type of adhesive, type of substrate, size and geometry of the substrate, and the precision requirement of the bond. The common application methods are spray, roll, curtain, and syringe or bead application. During application, volatile components are expected to evaporate, resulting in emissions to air. The application process may also generate process wastes, such as overspray, depending on the method used (OECD, 2015).

E.1.3.2 Automotive Care Products

D4 is present at less than 0.5 percent concentration in a leather and vinyl protector product. The product is used to preserve the appearance of leather and vinyl in cars, trucks and vans, and is available in an aerosol can (3M, 2019).

E.1.3.3 Furnishing, Cleaning, Treatment/Care Products

D4 is present as a residual (<1 percent) in several commercial laundry products, including laundry detergent and fabric softeners (Ecolab, 2019, 2017; Alpine Specialty Chemicals Ltd, 2016a, b). The use of laundry products typically results in down-the-drain releases to wastewater.

E.1.3.4 Ink, Toner, and Colorant Products

D4 is a component in several screen printing inks, at concentrations up to 2 percent (3M, 2018).

E.1.3.5 Laboratory Chemicals

D4 is used neat (90 percent concentration or higher) in laboratory settings, including as a gas chromatography (GC) reference standard; as a probe liquid for nuclear magnetic resonance cryoporometry (NMRC); and in the synthesis of other polymers such as PDMS (Sigma Aldrich, 2020; TCI America, 2019; Sigma Aldrich, 2018).

E.1.3.6 Paints and Coatings

D4 may be a component of paints and coatings, including automotive coating (B&B Blending LLC, 2019), wood floor finish (Buckeye International, 2018), and oil-based paint (Rust-Oleum Corporation, 2018). The concentration of D4 varies by product but was found to be as high as 55 percent in a type of automotive ceramic coating. This specific coating protects automobile from weather, chemicals, physical abrasion and UV rays, and provides water and dirt repellency (B&B Blending LLC, 2019).

The application method varies by product. For example, ceramic automotive coating can be applied by saturating a suede applicator with drops of coating material from a dripper bottle, and then applying to the vehicle using a cross-hatch pattern. The coating is then allowed to cure at ambient temperature (B&B Blending LLC, 2019). Floor finishes may be applied using a T-bar applicator (Buckeye International, 2018). Interior and exterior paints can be applied by roller, brush, or high-pressure airless spray gun (Rust-Oleum Corporation, 2018). In general, spray coating is the most common method to apply a liquid formulation to a surface (OECD, 2009b).

D4 may also be present as a residual (<1 percent) in various silicone-based coatings. The most prominent silicone coatings are pressure-sensitive adhesives, plastic hardcoats, and paper release coatings (Kirk-Othmer, 2008).

E.1.3.7 Plastic and Rubber Products

D4 is present as a residual in silicone polymer, which is then used to make a wide range of plastic and rubber products that may have industrial, commercial or consumer applications.

Silicone rubber is made by vulcanizing high molecular weight linear PDMS polymer (often called gum), which contains residual D4 monomer. The specific ratio of polymer, fillers, and cure catalysts can be customized to each application to provide the desired properties. Silicone rubber is most commonly fabricated by compression molding catalyzed gum stock at 100–180 °C under 5.5–10.3 Mpa. The materials are then extruded to form tubes, rods, wires, cable insulations, and articles with continuous profiles. Silicone rubber can also be processed through liquid injection molding (Rich et al., 2000).

E.1.4 Disposal

Each of the conditions of use of D4 may generate waste streams of the chemical that are collected and transported to third-party sites for disposal, treatment, or recycling. Industrial sites that treat or dispose on-site wastes that they themselves generate are assessed in each condition of use assessment. Similarly, point source discharges of D4 to surface water are assessed in each condition of use assessment (point source discharges are exempt as solid wastes under the Resource Conservation and Recovery Act (RCRA)). Wastes of D4 that are generated during a condition of use and sent to a third-party site for treatment, disposal, or recycling may include the following:

- Pursuant to section 304(a) of the Clean Water Act (CWA), EPA recommends water quality criteria pertaining to chemical pollutants in surface water to protect aquatic life or human health considering the designated uses of the surface water. Priority pollutants comprise a subset of these chemical substances, and the numbers of these priority pollutants are 103 and 25 in relation

to the protection of human health and aquatic life, respectively. States are required to adopt numeric criteria pertaining to priority pollutants according to the CWA if the discharge or presence of a priority pollutant could reasonably be expected to interfere with designated uses of the affected waters adopted by a state. Once these numeric criteria are adopted by a state and are approved by EPA, they become a part of the state's regulatory water quality standards. According to the CWA, National Pollutant Discharge Elimination System (NPDES) discharge permits must include effluent limits as stringent as necessary to meet a state's regulatory water quality standards. Furthermore, these effluent limits must also be as stringent as necessary to satisfy the technology-based effluent guidelines for the applicable source category (*e.g.*, D4 siloxane manufacturing is covered under the Organic Chemicals, Plastics, and Synthetic Fibers (OCPSF) point source category with effluent guidelines provided at 40 CFR part 414).

- D4 siloxane is not a regulated toxic pollutant (listed at 40 CFR 401.15) or priority pollutant (listed at 40 CFR part 423 Appendix A). However, state permit writers may consider issuing permit limits for chemicals not listed as toxic or priority pollutants; these chemicals are referred to as "nonconventional pollutants" in section 301(g) of the CWA. Discharge Monitoring Report (DMR) data are submitted by NPDES permit holders to the permitting authority (*i.e.*, the state or directly to EPA) in accordance with the monitoring requirements of the facility's permit. NPDES permit effluent limits are associated with approved monitoring analytical methods. Section 304(h) of the CWA directs EPA to promulgate these analytical methods, which are a requirement for making NPDES permit effluent limits enforceable, and these methods are published at 40 CFR part 136. Analytical method(s) pertaining to D4 siloxane have not been promulgated. Consequently, D4 siloxane has not been reported in the DMR data set for the past 15 years.

- Solid Wastes: Solid wastes are defined under RCRA as any material that is discarded by being: abandoned; inherently waste-like; a discarded military munition; or recycled in certain ways (certain instances of the generation and legitimate reclamation of secondary materials are exempted as solid wastes under RCRA). Solid wastes may subsequently meet RCRA's definition of hazardous waste by either being listed as a waste at 40 CFR 261.30 to 261.35 or by meeting waste-like characteristics as defined at 40 CFR 261.20 to 261.24. Solid wastes that are hazardous wastes are regulated under the more stringent requirements of Subtitle C of RCRA, whereas non-hazardous solid wastes are regulated under the less stringent requirements of Subtitle D of RCRA. Solid wastes containing D4 siloxane may be regulated as a hazardous waste under RCRA waste code D001 for ignitable liquids (40 CFR 261.21). D4 siloxane may also be comingled with solvent mixtures that are RCRA hazardous wastes. These wastes would be either incinerated in a hazardous waste incinerator or disposed to a hazardous waste landfill. Alternatively, D4 may be comingled with waste that is not RCRA hazardous waste and the resulting flash point of the mixture may no longer meet the ignitability criterion for RCRA waste code D001. D4 siloxane in consumer products may be disposed to municipal waste.

- Wastes Exempted as Solid Wastes under RCRA: Certain conditions of use of D4 may generate wastes of D4 that are exempted as solid wastes under 40 CFR 261.4(a).

E.2 Preliminary Occupational Exposure Data

NIOSH Health Hazard Evaluations (HHEs) have not been conducted with a focus on D4 monitoring and/or workplace exposure to date. D4 does not have an OSHA Integrated Management Information System (IMIS) code. As such, OSHA has not collected monitoring data for this chemical.

Appendix F SUPPORTING INFORMATION – CONCEPTUAL MODEL FOR INDUSTRIAL AND COMMERCIAL ACTIVITIES AND USES

Table_Apx F-1. Worker and Occupational Non-user Exposure Conceptual Model Supporting Table

Life Cycle Stage	Category	Subcategory	Release / Exposure Scenario	Exposure Pathway	Exposure Route	Receptor / Population	Plans to Evaluate	Rationale
Manufacturing	Manufacturing Import	Manufacturing Import	Manufacture of D4 Repackaging of import containers	Liquid Contact	Dermal	Worker	Yes	Workers may have dermal contact with liquids during manufacturing and import activities.
				Solid	Dermal	Worker	Yes	According to the 2016 CDR, D4 may be imported in dry powder form. Dermal contact with solids may occur when D4 is imported as dry powder.
				Liquid/ Solid Contact	Dermal	ONU	No	Dermal exposure is expected to be primarily to workers who directly handle the chemical.
				Vapor	Inhalation	Worker	Yes	D4 is a semi-volatile liquid. Inhalation exposure to vapor should be further evaluated.
				Vapor	Inhalation	ONU	Yes	
				Dust	Inhalation	Worker / ONU	Yes	According to the 2016 CDR, D4 may be imported in dry powder form. Inhalation to dust may occur during solids transferring activities.
				Solid (Settled Dust)	Dermal	Worker/ ONU	Yes	Dust may settle on surfaces that workers or ONUs may touch.
Processing	Processing as a reactant	Adhesives and sealant chemicals All other basic inorganic chemical mfg. All other basic organic chemical mfg. All other	Processing of D4 as a reactant, precursor, or monomer (incl. processing of D4 to produce silicone polymers)	Liquid Contact	Dermal	Worker	Yes	Workers may have dermal contact with liquids during activities such as container unloading, equipment maintenance and cleaning.
				Solid	Dermal	Worker	Yes	D4 may be present in a solid powder formulation. Dermal contact with solids may occur during unloading and transferring activities.
				Liquid/ Solid Contact	Dermal	ONU	No	Dermal exposure is expected to be primarily to workers who directly handle the chemical.
				Vapor	Inhalation	Worker	Yes	

Life Cycle Stage	Category	Subcategory	Release / Exposure Scenario	Exposure Pathway	Exposure Route	Receptor / Population	Plans to Evaluate	Rationale
		chemical pdt and preparation mfg. Synthetic rubber mfg. Plastic material and resin mfg.		Vapor	Inhalation	ONU	Yes	D4 is a semi-volatile liquid. Inhalation exposure to vapor should be further evaluated.
				Dust	Inhalation	Worker	Yes	D4 may be present in a solid powder formulation. Inhalation to dust may occur during solids transferring activities.
				Dust	Inhalation	ONU	Yes	
				Solid (Settled Dust)	Dermal	Worker/ ONU	Yes	Dust may settle on surfaces that workers or ONUs may touch.
Processing	Incorporation into formulation, mixture, or reaction product	All other basic inorganic chem mfg.; All other chem pdt and prep mfg.; Cyclic crude and intermediate mfg.; Misc mfg.; product mfg.; Paint and coating mfg; Asphalt paving, roofing, and coating materials mfg.	Processing of silicone polymer containing D4 to produce other chemicals and products	Liquid Contact	Dermal	Worker	Yes	Workers may have dermal contact with liquids during processing and use of silicone polymer products containing D4.
				Liquid Contact	Dermal	ONU	No	Dermal exposure is expected to be primarily to workers who directly handle the chemical.
				Vapor	Inhalation	Worker	Yes	D4 is semi-volatile liquid and may continue to evaporate after incorporated into polymers and other products. Inhalation exposure to vapor should be further evaluated.
				Vapor	Inhalation	ONU	Yes	
Processing	Incorporation into formulation, mixture, or reaction product	Computer and electronic product mfg. Electrical equipment, appliance, and component mfg.	Processing of silicone polymer containing D4 to produce electronics encapsulant or coating	Liquid Contact	Dermal	Worker	Yes	Workers may have dermal contact with liquids during processing and use of silicone polymer products containing D4.
				Liquid Contact	Dermal	ONU	No	Dermal exposure is expected to be primarily to workers who directly handle the chemical.
				Vapor	Inhalation	Worker	Yes	D4 is semi-volatile liquid and may continue to evaporate after incorporated into polymers and other products. Inhalation exposure to vapor should be further evaluated.
				Vapor	Inhalation	ONU	Yes	

Life Cycle Stage	Category	Subcategory	Release / Exposure Scenario	Exposure Pathway	Exposure Route	Receptor / Population	Plans to Evaluate	Rationale
Processing	Incorporation into formulation, mixture, or reaction product	Rubber product manufacturing Synthetic rubber manufacturing	Processing of silicone polymer containing D4 to produce silicone rubber compounds	Liquid Contact	Dermal	Worker	Yes	Workers may have dermal contact with liquids during processing and use of silicone polymer products containing D4.
				Liquid Contact	Dermal	ONU	No	Dermal exposure is expected to be primarily to workers who directly handle the chemical.
				Vapor	Inhalation	Worker	Yes	D4 is semi-volatile liquid and may continue to evaporate after incorporated into polymers and other products. Inhalation exposure to vapor should be further evaluated.
				Vapor	Inhalation	ONU	Yes	
Processing	Processing – Repackaging	All other basic inorganic chem mfg. All other chem pdt and prep mfg.	Repackaging to large and small containers	Liquid Contact	Dermal	Worker	Yes	Workers may have dermal contact with liquids during packaging, equipment maintenance and cleaning activities.
				Liquid Contact	Dermal	ONU	No	Dermal exposure is expected to be primarily to workers who directly handle the chemical.
				Vapor	Inhalation	Worker	Yes	D4 is a semi-volatile liquid. Inhalation exposure to vapor should be further evaluated.
				Vapor	Inhalation	ONU	Yes	
Distribution	Distribution in commerce	Distribution in commerce	Distribution of bulk shipments of D4 and formulated products	Liquid / Solid Contact, Vapor	Dermal, Inhalation	Worker ONU	Yes	EPA plans to analyze activities resulting in exposures associated with distribution in commerce (*e.g.*, loading, unloading) throughout the various life cycle stages and conditions of use (*e.g.*, manufacturing, processing, industrial use, commercial use, disposal) rather than a single distribution scenario.
Commercial uses	Adhesives and sealants Automotive care products	Adhesives and sealants Automotive care products	Use of adhesives and sealants Use of automotive care products (*e.g.*,	Liquid Contact	Dermal	Worker	Yes	Workers may have dermal contact with liquids when using silicone polymer products containing D4.
				Liquid Contact	Dermal	ONU	No	Dermal exposure is expected to be primarily to workers who directly handle the chemical.
				Vapor	Inhalation	Worker	Yes	

Life Cycle Stage	Category	Subcategory	Release / Exposure Scenario	Exposure Pathway	Exposure Route	Receptor / Population	Plans to Evaluate	Rationale
			leather and vinyl protector)	Vapor	Inhalation	ONU	Yes	Inhalation exposure from volatilization of D4 residue in silicone polymer should be further evaluated.
				Mist	Inhalation	Worker	Yes	Workers may be exposed to mist if products are spray-applied
				Liquid (Settled Mist)	Dermal	Worker/ ONU	Yes	Dermal exposure to liquid films resulting from the settling of mist should be further evaluated.
	Furnishing, Cleaning, Treatment/Care Products	Fabric, textile, and leather products not covered elsewhere Cleaning and furnishing care products	Use of cleaning and laundry products (*e.g.*, detergent, fabric softener)	Liquid Contact	Dermal	Worker	Yes	Workers may have dermal contact with liquids when using silicone polymer products containing D4.
				Liquid Contact	Dermal	ONU	No	Dermal exposure is expected to be primarily to workers who directly handle the chemical.
				Vapor	Inhalation	Worker	Yes	Inhalation exposure from volatilization of D4 residue in silicone polymer should be further evaluated.
				Vapor	Inhalation	ONU	Yes	

Life Cycle Stage	Category	Subcategory	Release / Exposure Scenario	Exposure Pathway	Exposure Route	Receptor / Population	Plans to Evaluate	Rationale
Commercial uses	Ink, Toner, and Colorant Products	Ink, Toner, and Colorant Products	Screen printing	Liquid Contact	Dermal	Worker	Yes	Workers may have dermal exposure when transferring ink to printers or during the printing process.
				Liquid Contact	Dermal	ONU	No	Dermal exposure is expected to be primarily to workers who directly handle the chemical.
				Vapor	Inhalation	Worker	Yes	Inhalation exposure from volatilization of D4 residue in silicone polymer should be further evaluated.
				Vapor	Inhalation	ONU	Yes	
				Mist	Inhalation	Worker	Yes	Mist exposure is expected from high-speed web-fed presses.
				Liquid (Settled Mist)	Dermal	Worker/ ONU	Yes	Dermal exposure to liquid films resulting from the settling of mist should be further evaluated.
	Laboratory chemicals	Laboratory chemicals [d]	Use of D4 in laboratories (*e.g.*, reference standard)	Liquid Contact	Dermal	Worker	Yes	Workers may have dermal contact with liquids when using D4 in laboratories.
				Liquid Contact	Dermal	ONU	No	Dermal exposure is expected to be primarily to workers who directly handle the chemical.
				Vapor	Inhalation	Worker	Yes	D4 is semi-volatile liquid. Inhalation exposure to vapor should be further evaluated.
				Vapor	Inhalation	ONU	Yes	
Commercial uses	Paints and coatings	Paints and coatings	Application of paints and coatings	Liquid Contact	Dermal	Worker	Yes	Workers may have dermal contact with liquids when using silicone polymer products containing D4.
				Liquid Contact	Dermal	ONU	No	Dermal exposure is expected to be primarily to workers who directly handle the chemical.
				Vapor	Inhalation	Worker	Yes	Inhalation exposure from volatilization of D4 residue in silicone polymer should be further evaluated.
				Vapor	Inhalation	ONU	Yes	
				Mist	Inhalation	Worker	Yes	Workers may be exposed to mist if paints and coatings are spray-applied
				Liquid (Settled Mist)	Dermal	Worker/ ONU	Yes	Dermal exposure to liquid films resulting from the settling of mist should be further evaluated.
	Plastic and rubber products not	Plastic and rubber products not	Use of plastic and rubber products	Solid (migration	Dermal	Worker	Yes	Workers may have dermal contact with silicone-based products and articles, and dermal exposure resulting

Life Cycle Stage	Category	Subcategory	Release / Exposure Scenario	Exposure Pathway	Exposure Route	Receptor / Population	Plans to Evaluate	Rationale
	covered elsewhere	covered elsewhere		of D4 from an article)				from migration of D4 from an article should be further evaluated.
				Solid	Dermal	ONU	No	Dermal exposure is expected to be primarily to workers who directly handle the chemical.
				Vapor	Inhalation	Worker	Yes	Inhalation exposure from volatilization of D4 residue in silicone polymer should be further evaluated.
				Vapor	Inhalation	ONU	Yes	
Disposal	Disposal	Waste handling, treatment, and disposal	Exposure occuring during disposal	Liquid Contact	Dermal	Worker	Yes	Workers may have dermal contact with liquids when handling wastes containing D4.
				Liquid Contact	Dermal	ONU	No	Dermal exposure is expected to be primarily to workers who directly handle the chemical.
				Vapor	Inhalation	Worker	Yes	D4 is semi-volatile liquid. Inhalation exposure to vapor should be further evaluated.
				Vapor	Inhalation	ONU	Yes	
				Dust	Inhalation	Worker/ ONU	Yes	D4 vapor that is generated my adsorb on dust particles in a landfill or else dust containing D4 may be generated during landfilling operations.

Appendix G SUPPORTING INFORMATION – CONCEPTUAL MODEL FOR CONSUMER ACTIVITIES AND USES

Table_Apx G-1. Consumer Exposure Conceptual Model Supporting Table

Life Cycle Stage	Category	Subcategory	Release from Source	Exposure Pathway	Route	Receptor	Plans to Evaluate	Rationale
Consumer Use	Furnishing, Cleaning, Treatment/Care Products	Fabric, textile, and leather products not covered elsewhere (Article)	Direct contact through handling of articles containing chemical	Direct Contact	Dermal	Consumers	Yes	Dermal exposure may occur for this condition of use
			Direct contact through mouthing of articles containing chemical	Mouthing	Oral	Consumers	Yes	Oral exposure may occur for this condition of use
			Long-term emission/mass-transfer, Abrasion, Transfer to Dust	Dust	Dermal, Inhalation, Oral	Consumers, Bystanders	Yes	Dermal, oral, and inhalation exposure from this condition of use may occur
			Long-term emission/mass-transfer through application or use of products	Vapor	Inhalation Oral	Consumers, Bystanders	Yes	Inhalation and incidental ingestion are possible.
Consumer Use	Packaging, Paper, Plastic, Hobby Products	Plastic and rubber products not covered elsewhere (Article)	Direct contact through handling of articles containing chemical	Direct Contact	Dermal	Consumers	Yes	Dermal exposure may occur for this condition of use
			Direct contact through mouthing of articles containing chemical	Mouthing	Oral	Consumers	Yes	Oral exposure may occur for this condition of use
			Long-term emission/mass-transfer, Abrasion, Transfer to Dust	Dust	Dermal, Inhalation, Oral	Consumers, Bystanders	Yes	Dermal, oral, and inhalation exposure from this condition of use may occur
			Long-term emission/mass-transfer through	Vapor	Inhalation Oral	Consumers, Bystanders	Yes	Inhalation and incidental ingestion are possible.

Life Cycle Stage	Category	Subcategory	Release from Source	Exposure Pathway	Route	Receptor	Plans to Evaluate	Rationale
			application or use of products					
Consumer Use	Packaging, Paper, Plastic, Hobby Products	Toys, Playground, and Sporting Equipment (Article)	Direct contact through handling of articles containing chemical	Direct Contact	Dermal	Consumers	Yes	Dermal exposure may occur for this condition of use
			Direct contact through mouthing of articles containing chemical	Mouthing	Oral	Consumers	Yes	Oral exposure may occur for this condition of use
			Long-term emission/mass-transfer, Abrasion, Transfer to Dust	Dust	Dermal, Inhalation, Oral	Consumers, Bystanders	Yes	Dermal, oral, and inhalation exposure from this condition of use may occur
			Long-term emission/mass-transfer through application or use of products	Vapor	Inhalation Oral	Consumers, Bystanders	Yes	Inhalation and incidental ingestion are possible.
Consumer Use	Adhesives and sealants	Adhesives and Sealants (Product)	Long-term emission/mass-transfer, Abrasion, Transfer to Dust	Dust	Dermal, Inhalation, Oral	Consumers, Bystanders	Yes	Dermal, oral, and inhalation exposure from this condition of use may occur.
			Direct contact through application or use of products	Liquid Contact	Dermal	Consumers	Yes	Exposure is expected to be primarily restricted to consumer who are directly involved in using the chemical.
			Long-term emission/mass-transfer through application or use of products	Vapor	Inhalation Oral	Consumers, Bystanders	Yes	Inhalation and incidental ingestion are possible.
			Direct contact through application or use of products	Mist	Inhalation, Dermal, Oral	Consumers, Bystanders	Yes	If product is applied as a mist, inhalation, dermal, and oral exposure would be expected.

Life Cycle Stage	Category	Subcategory	Release from Source	Exposure Pathway	Route	Receptor	Plans to Evaluate	Rationale
Consumer Use	Automotive care products	Automotive Care Products (Product)	Long-term emission/mass-transfer, Abrasion, Transfer to Dust	Dust	Dermal, Inhalation, Oral	Consumers, Bystanders	Yes	Dermal, oral, and inhalation exposure from this condition of use may occur.
			Direct contact through application or use of products	Liquid Contact	Dermal	Consumers	Yes	Exposure is expected to be primarily restricted to consumer who are directly involved in using the chemical.
			Long-term emission/mass-transfer through application or use of products	Vapor	Inhalation Oral	Consumers, Bystanders	Yes	Inhalation and incidental ingestion are possible.
			Direct contact through application or use of products	Mist	Inhalation, Dermal, Oral	Consumers, Bystanders	Yes	If product is applied as a mist, inhalation, dermal, and oral exposure would be expected.
Consumer Use	Furnishing, Cleaning, Treatment/Care Products	Cleaning and furnishing care products (Product)	Long-term emission/mass-transfer, Abrasion, Transfer to Dust	Dust	Dermal, Inhalation, Oral	Consumers, Bystanders	Yes	Dermal, oral, and inhalation exposure from this condition of use may occur.
			Direct contact through application or use of products	Liquid Contact	Dermal	Consumers	Yes	Exposure is expected to be primarily restricted to consumer who are directly involved in using the chemical.
			Long-term emission/mass-transfer through application or use of products	Vapor	Inhalation Oral	Consumers, Bystanders	Yes	Inhalation and incidental ingestion are possible.
			Direct contact through application or use of products	Mist	Inhalation, Dermal, Oral	Consumers, Bystanders	Yes	If product is applied as a mist, inhalation, dermal, and oral exposure would be expected.
Consumer Use	Furnishing, Cleaning, Treatment/Care Products	Fabric, textile, and leather products not covered	Direct contact through handling of products containing chemical	Direct Contact	Dermal	Consumers	Yes	Dermal exposure may occur for this condition of use

Life Cycle Stage	Category	Subcategory	Release from Source	Exposure Pathway	Route	Receptor	Plans to Evaluate	Rationale
		elsewhere (Product)	Direct contact through mouthing of products containing chemical	Mouthing	Oral	Consumers	Yes	Oral exposure may occur for this condition of use
			Long-term emission/mass-transfer, Abrasion, Transfer to Dust	Dust	Dermal, Inhalation, Oral	Consumers, Bystanders	Yes	Dermal, oral, and inhalation exposure from this condition of use may occur
			Long-term emission/mass-transfer through application or use of products	Vapor	Inhalation Oral	Consumers, Bystanders	Yes	Inhalation and incidental ingestion are possible.
Consumer Use	Furnishing, Cleaning, Treatment/Care Products	Laundry and dishwashing products (Product)	Direct contact through application or use of products	Mist	Inhalation, Dermal, Oral	Consumers, Bystanders	Yes	If product is applied as a mist, inhalation, dermal, and oral exposure would be expected.
			Direct contact through application or use of products	Liquid Contact	Dermal	Consumers	Yes	Exposure is expected to be primarily restricted to consumer who are directly involved in using the chemical.
			Long-term emission/mass-transfer through application or use of products	Vapor	Inhalation Oral	Consumers, Bystanders	Yes	Inhalation and incidental ingestion are possible.
Consumer Use	Other	Animal Grooming Products	Direct contact through application or use of products	Liquid Contact	Dermal	Consumers	Yes	Exposure is expected to be primarily restricted to consumer who are directly involved in using the chemical.
			Long-term emission/mass-transfer through application or use of products	Vapor	Inhalation Oral	Consumers, Bystanders	Yes	Inhalation and incidental ingestion are possible.
			Direct contact through application or use of products	Mist	Inhalation, Dermal, Oral	Consumers, Bystanders	Yes	If product is applied as a mist, inhalation, dermal, and oral exposure would be expected.

Life Cycle Stage	Category	Subcategory	Release from Source	Exposure Pathway	Route	Receptor	Plans to Evaluate	Rationale
Consumer Use	Paints and coatings	Paints and Coatings (Product)	Long-term emission/mass-transfer, Abrasion, Transfer to Dust	Dust	Dermal, Inhalation, Oral	Consumers, Bystanders	Yes	Dermal, oral, and inhalation exposure from this condition of use may occur.
			Direct contact through application or use of products	Liquid Contact	Dermal	Consumers	Yes	Exposure is expected to be primarily restricted to consumer who are directly involved in using the chemical.
			Long-term emission/mass-transfer through application or use of products	Vapor	Inhalation Oral	Consumers, Bystanders	Yes	Inhalation and incidental ingestion are possible.
			Direct contact through application or use of products	Mist	Inhalation, Dermal, Oral	Consumers, Bystanders	Yes	If product is applied as a mist, inhalation, dermal, and oral exposure would be expected.
Consumer Use	Packaging, Paper, Plastic, Hobby Products	Plastic and rubber products not covered elsewhere (Product)	Direct contact through handling of products containing chemical	Direct Contact	Dermal	Consumers	Yes	Dermal exposure may occur for this condition of use
			Direct contact through mouthing of products containing chemical	Mouthing	Oral	Consumers	Yes	Oral exposure may occur for this condition of use
			Long-term emission/mass-transfer, Abrasion, Transfer to Dust	Dust	Dermal, Inhalation, Oral	Consumers, Bystanders	Yes	Dermal, oral, and inhalation exposure from this condition of use may occur
			Long-term emission/mass-transfer through application or use of products	Vapor	Inhalation Oral	Consumers, Bystanders	Yes	Inhalation and incidental ingestion are possible.
Consumer Use	Packaging, Paper, Plastic, Hobby Products	Toys, Playground, and Sporting	Direct contact through handling of products containing chemical	Direct Contact	Dermal	Consumers	Yes	Dermal exposure may occur for this condition of use

Life Cycle Stage	Category	Subcategory	Release from Source	Exposure Pathway	Route	Receptor	Plans to Evaluate	Rationale
		Equipment (Product)	Direct contact through mouthing of products containing chemical	Mouthing	Oral	Consumers	Yes	Oral exposure may occur for this condition of use
			Long-term emission/mass-transfer, Abrasion, Transfer to Dust	Dust	Dermal, Inhalation, Oral	Consumers, Bystanders	Yes	Dermal, oral, and inhalation exposure from this condition of use may occur
			Long-term emission/mass-transfer through application or use of products	Vapor	Inhalation Oral	Consumers, Bystanders	Yes	Inhalation and incidental ingestion are possible.
Consumer Handling of Disposal and Waste	Wastewater, liquid wastes, and solid wastes	Wastewater, liquid wastes, and solid wastes	Long-term emission/mass-transfer, Abrasion, Transfer to Dust	Dust	Dermal, Inhalation, Oral	Consumers, Bystanders	Yes	Dust generation is possible during the handling of solid waste.
			Direct contact through handling or disposal of products	Liquid Contact	Dermal	Consumers	Yes	Exposure is expected to be primarily restricted to consumers who are directly involved in handling and disposal of the chemical.
			Long-term emission/mass-transfer through application or use of products	Vapor	Inhalation Oral	Consumers, Bystanders	Yes	Inhalation and incidental ingestion are possible.
			Direct contact through application or use of products	Mist	Inhalation, Dermal, oral	Consumers, Bystanders	No	Mist generation is not expected during the handling or disposal

Appendix H SUPPORTING INFORMATION – CONCEPTUAL MODEL FOR ENVIRONMENTAL RELEASES AND WASTES

Table_Apx H-1. General Population and Environmental Exposure Conceptual Model Supporting Table

Life Cycle Stage	Category	Release	Exposure Pathway / Media	Exposure Routes	Receptor / Population	Plans to Evaluate	Rationale
All	Emissions to Air	Emissions to Air	Near facility ambient air concentrations	Inhalation	General Population	Yes	D4 deposition to nearby bodies of water and soil are expected exposure pathways, not covered under other EPA regulations, and, therefore in scope.
			Indirect deposition to nearby bodies of water and soil catchments	Oral Dermal	General Population	Yes	
				TBD	Aquatic and Terrestrial Receptors	Yes	
	Wastewater or Liquid Wastes	Industrial pre-treatment and wastewater treatment, or POTW	Direct release into surface water and indirect partitioning to sediment	TBD	Aquatic and Terrestrial Receptors	Yes	Release of D4 into surface water and indirect partitioning to sediment exposure pathways to aquatic and terrestrial receptors will be analyzed
				Oral Dermal	General Population	Yes	Release of D4 into surface water and indirect partitioning to sediment and bioaccumulation exposure pathways to the general population will be analyzed.
			Drinking Water via Surface or Groundwater	Oral Dermal and Inhalation (*e.g.*, showering)	General Population	Yes	Release of D4 into surface water and indirect partitioning to drinking water is an expected exposure pathway.

Life Cycle Stage	Category	Release	Exposure Pathway / Media	Exposure Routes	Receptor / Population	Plans to Evaluate	Rationale
			Biosolids: application to soil and/or migration to groundwater and/or surface water	Oral (*e.g.*, ingestion of soil) Inhalation	General Population	Yes	EPA plans to analyze the pathway from biosolids to the general population, aquatic and terrestrial species.
				TBD	Aquatic and Terrestrial Receptors	Yes	
			Air	Inhalation	General Population	Yes	EPA plans to analyze the pathway from municipal landfills and other land disposal to the general population, receptors.
Disposal	Solid and Liquid Wastes	Municipal landfill and other land disposal	Leachate to soil, groundwater and/or migration to surface water	Oral Dermal	General Population	Yes	EPA plans to analyze the pathway from municipal landfills and other land disposal to the general population, aquatic and terrestrial receptors.
				TBD	Aquatic and Terrestrial Receptors		
			Air	Inhalation	General Population	Yes	EPA plans to analyze the pathway from municipal landfills and other land disposal to the general population, receptors.