Supporting Information for Low-Priority Substance Tetracosane, 2,6,10,15,19,23-Hexamethyl- (CASRN 111-01-3) (Squalane)

Final Designation

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1. Introduction

The Lautenberg amendments to the Toxic Substances Control Act (TSCA) require EPA to designate chemical substances as either High-Priority Substances for risk evaluation, or Low-Priority Substances for which risk evaluations are not warranted at this time (section 6(b)(1)(B) and implementing regulations (40 CFR 702.3)). A high-priority substance is defined as a chemical substance that the Administrator concludes, without consideration of costs or other non-risk factors, may present an unreasonable risk of injury to health or the environment because of a potential hazard and a potential route of exposure under the conditions of use, including an unreasonable risk to potentially exposed or susceptible subpopulations identified as relevant by the Administrator. If the Administrator concludes, based on information sufficient to establish, without consideration of costs or other non-risk factors, that the high-priority standard is not met, then the substance must be designated as a low-priority substance. Tetracosane, 2,6,10,15,19,23-hexamethyl-, referenced as squalane for the remainder of this document, is one of the 40 chemical substances initiated for prioritization as referenced in a March 21, 2019 notice (84 FR 10491)[1] and one of the 20 proposed as low-priority substances in an August 15, 2019 notice (84 FR 41712).[2]

As described under EPA's regulations at 40 CFR 702.9[3] and pursuant to section 6(b)(1)(A) of the statute, EPA generally used reasonably available information to screen the chemical substance under its conditions of use against the following criteria and considerations:

- the hazard and exposure potential of the chemical substance;
- persistence and bioaccumulation;
- potentially exposed or susceptible subpopulations;
- storage near significant sources of drinking water;
- conditions of use or significant changes in the conditions of use of the chemical substance;
- the chemical substance's production volume or significant changes in production volume; and
- other risk-based criteria that EPA determines to be relevant to the designation of the chemical substance's priority.

Designation of a low-priority substance is not a finding that the chemical substance does not present an unreasonable risk, but rather that the chemical substance does not meet the statutory criteria for a high-priority substance and that a risk evaluation is not warranted at the time. As explained in the preamble to the Prioritization Rule, "low-priority substance designations give the public notice of chemical substances for which the hazard and/or exposure potential is anticipated to be low or nonexistent and provides some insight into which chemical substances are likely not to need additional evaluation and risk management under TSCA." 82 FR 33753 at 33755. EPA is not precluded from later revising the designation based on reasonably available information, if warranted. 40 CFR 702.13; 702.15.

[1] https://www.federalregister.gov/documents/2019/03/21/2019-05404/initiation-of-prioritization-under-the-toxic-substances-control-act-tsca

[2] https://www.federalregister.gov/documents/2019/08/15/2019-17558/proposed-low-priority-substance-designation-under-the-toxic-substances-control-act-tsca-notice-of

[3] The prioritization process is explained in the *Procedures for Prioritization of Chemicals for Risk Evaluation Under the Toxic Substances Control Act* (82 FR 33753).

The screening review is not a risk evaluation, but rather a review of reasonably available information on the chemical substance that relates to the specific criteria and considerations in TSCA section 6(b)(1)(A) and 40 CFR 702.9. This paper documents the results of the screening review which supports the final designation of squalane as a low-priority substance. EPA has also prepared a general response to comments and, as applicable, chemical-specific responses to comments.

This risk-based, screening-level review is organized as follows:

- *Section 1 (Introduction):* This section explains the requirements of the Lautenberg amendments to the Toxic Substances Control Act (TSCA) and implementing regulations – including the criteria and considerations -- pertinent to prioritization and designation of low-priority substances.

- *Section 2 (Background on the Low-Priority Substance):* This section includes information on attributes of the chemical substance, including its structure, and relates them to its functionality.

- *Section 3 (Physical-Chemical Properties):* This section includes a description of the physical-chemical properties of the chemical substance and explains how these properties lead to the chemical's fate, transport, and exposure potential.

- *Section 4 (Relevant Assessment History):* This section includes an overview of the outcomes of other governing entities' assessments of the chemical substance.

- *Section 5 (Conditions of Use):* This section presents the chemical substance's known, intended, and reasonably foreseen conditions of use under TSCA.

- *Section 6 (Hazard Characterization):* This section summarizes the reasonably available hazard information and screens the information against low-concern benchmarks.

- *Section 7 (Exposure Characterization):* This section includes a qualitative summary of potential exposures to the chemical substance.

- *Section 8 (Summary of Findings):* In this section, EPA presents information pertinent to prioritization against each of the seven statutory and regulatory criteria and considerations, and makes a conclusion based on that evidence.

- *Section 9 (Final Designation):* In this section, EPA presents the final designation for this chemical substance.

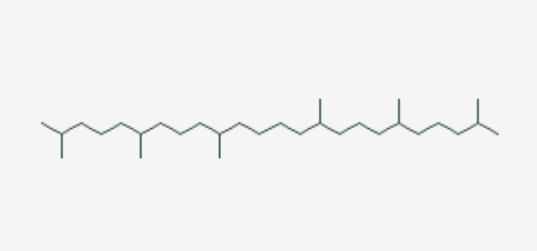
- *Appendix A (Conditions of Use Characterization):* This appendix contains a comprehensive list of TSCA and non-TSCA uses for the chemical substance from publicly available databases.

- *Appendix B (Hazard Characterization):* This appendix contains information on each of the studies used to support the hazard evaluation of the chemical substance.

- *Appendix C (Literature Search Outcomes):* This appendix includes literature search outcomes and rationales for studies that were identified in initial literature screening but were found to be off-topic or unacceptable for use in the screening-level review.

2. Background on Squalane

Table 1 below provides the CAS number, synonyms, and other information on squalane.

Table 1: Squalane at a Glance	
Chemical Name	Squalane
CASRN	111-01-3
Synonyms	Tetracosane, 2,6,10,15,19,23-hexamethyl-; 2,6,10,15,19,23-Hexamethyltetracosane; Hexamethyl tetracosane; Tetracosane,6,10,15,19,23-hexamethyl-; Squalane (Polyquaternium-39); Cosbiol; Perhydrosqualene; Dodecahydrosqualene
Trade Name(s)	Evoil; Neossance; Robane; Spinacane, Vitabiosol
Molecular Formula	$C_{30}H_{62}$
Representative Structure	

Squalane is a saturated hydrocarbon oil that is formed by the hydrogenation of squalene. Its structure is composed of a 24-carbon chain substituted with six methyl groups in the 2, 6, 10, 15, 19, and 23 positions. Squalane can be found in small quantities in sebum, a natural substance that acts as an antioxidant and protects the skin from bacteria while keeping it hydrated. Squalene is most commonly found in nature as a lipid in both plants and animals, most notably in shark livers, olive oil, rice, and sugar cane. Section 5 includes conditions of use for this chemical.

3. Physical-Chemical Properties

Table 2 lists the physical-chemical properties for squalane. A chemical's physical-chemical properties provide a basis for understanding a chemical's behavior, including in the environment and in living organisms. These endpoints provide information generally needed to assess potential environmental release, exposure, and partitioning as well as insight into the potential for adverse toxicological effects.

Table 2: Physical-Chemical Properties for Squalane

Source/ Model	Data Type	Endpoint	Endpoint value	Notes
Sigma-Aldrich 2019	Experimental	Physical state at room temperature (based on melting point)	Liquid (-38°C)	
Reported to the ECHA database 2018	Experimental	Molecular weight	423 g/mol	
EPISuite v.4.11[4]	Calculated	Molecular weight	422.83 g/mol	
Lyman et al. 1990	Experimental	Molar volume	673.4 cm^3/mol	LeBas Molar Volume, calculated according to the volume parameters reported in Lyman et al. 1990
PubChem 2020	Experimental (analog)	Water solubility	$1x10^{-8}$ mg/L	Water solubility data are not available for squalane. This value represents experimental data for analog pentadecane, 1,6,10,14-tetramethyl- (CASRN 1921-70-6), Squalane is larger and therefore is expected to be more hydrophobic than this analog, resulting in a lower water solubility.
Reported to the ECHA database 2018	Experimental	Water solubility	$1.42x10^{-5}$ mol/L; $2.37x10^{-6}$ mol/L ; $7.10x10^{-6}$ mol/L	
Reported to the ECHA database 2018	Experimental	Log K_{ow}	5.49 at 20 deg C and pH 6.4	The measured octanol-water partition coefficient is most likely underestimated by the test method (OECD 107). Study authors noted that squalane is completely soluble in octanol (> 10,000 g/L), but that in water, the chemical is very weakly soluble and that the solubility is under the detection limit.
EPISuite v.4.11	Estimated	Log K_{ow}	> 8	Estimated via EPISuite; however, EPA determined that squalane is outside the applicability domain of the model.

[4] EPI Suite (Physical Property Inputs - BP = 350ºC, MP = -38ºC), SMILES: CC(C)CCCC(C)CCCC(C)CCCCC(C)CCCC(C)CCCC(C)C

Table 2: Physical-Chemical Properties for Squalane				
Source/ Model	**Data Type**	**Endpoint**	**Endpoint value**	**Notes**
EPISuite v.4.11	Estimated	Log K_{oa}	9.83	Estimated via EPISuite; however, EPA determined that squalane is outside the applicability domain of the model.
EPISuite v.4.11	Estimated	Log K_{oc}	8.0 (MCI); 12.7 (K_{ow})	Estimated via EPISuite; however, EPA determined that squalane is outside the applicability domain of the model.
Reported to the ECHA database 2018	Experimental	Vapor pressure	$3.6x10^{-10}$ mm Hg ($4.8x10^{-8}$ Pa at 20°C)	
EPISuite v.4.11	Estimated	Vapor pressure	$2.75x10^{-4}$ mm Hg	
EPISuite v.4.11	Estimated	Henry's Law	1500 atm-m^3/mole	
EPISuite v.4.11	Estimated	Volatilization	2.1 hours (river) 195 hours (lake)	
EPISuite v.4.11	Estimated	Photolysis (indirect)	3.17 hours ($T_{1/2}$)	• OH rate constant 4.05E-11 cm^3/molecules-second (12-hour day; 1.5E6 OH/cm^3) • No ozone reaction estimation
Ruehl et al. 2013	Estimated based on experimental data	Photooxidation ($T_{1/2}$)	6.7 days	• Hydroxyl radical decay rate constant = 1.6±0.4E-12 cm^3/molecules-second (12-hour day; 1.5E6 OH/cm^3)
EPISuite v.4.11	Estimated	Hydrolysis	Rate constants cannot be estimated	No hydrolyzable functional groups
EPISuite v.4.11	Estimated	Biodegradation potential	Ready prediction: No	
EPISuite v.4.11	Estimated	Wastewater treatment plant removal	99.9% Total Removal (88.8% biodegradation, 11.2% sludge, 0% air)	Input parameters: BioP = 4, BioA = 1, and BioS = 1 based on 77% degradation after 28 days (10-day window met) by CO2 evolution, in OECD 301B test
Cravedi and Tulliez 1986	Calculated based on experimental data	BMF_k	0.0059	Calculation based on OECD Guideline 305, annex 7; see Section 6.3.2 and Appendix B for details
Cravedi and Tulliez 1986	Calculated based on experimental data	BMF_{kg}	0.12	Calculation based on OECD Guideline 305, annex 7; see Section 6.3.2 and Appendix B for details

EPA's Sustainable Futures/P2 Framework Manual[5] was used to interpret the physical-chemical properties provided in Table 2. Based on its reported physical state and melting point, squalane is a liquid at ambient temperatures. Liquids have the potential for exposure via direct dermal contact with the substance, ingestion, and by inhalation of aerosols, if they are generated. Based on its experimental vapor pressure (Reported to the ECHA database, 2018), squalane is not volatile under ambient conditions, minimizing the potential for exposure through inhalation of vapors. Further, if aerosols are generated, absorption across the lungs is unlikely. Based on its estimated water solubility, squalane is insoluble in water (Reported to the ECHA database, 2018). Given its low water solubility, this chemical is unlikely to be absorbed dermally or from the gastrointestinal tract. The estimated log K_{ow} indicates that squalane is not likely to be bioavailable, and it has low potential for absorption and sequestration in fatty tissue, as confirmed by its calculated BMFs (see Section 6.3.2). Squalane's estimated log K_{oc} indicates squalane is likely to adsorb to sediment and soil particles (EPISuite v4.11). It is predicted to be immobile in soil, which along with its water insolubility, shows a decreased potential to contaminate groundwater, including well water. Experimental biodegradation data indicate that squalane is biodegradable in aerobic conditions (discussed further in Section 6.3.1), meaning this chemical is not persistent and it has the potential to be broken down into carbon dioxide and water.

3.1 References

Cravedi JP, Tulliez J 1986; Environmental Pollution (Series A). Ecological and Biological 42: 247-59.

European Chemicals Agency (ECHA). (2018). 2,6,10,15,19,23-hexamethyltetracosane. Retrieved from https://echa.europa.eu/registration-dossier/-/registered-dossier/14412

Lyman, Warren J., Reehl, W. F., Rosenblatt, D. H. (1990). Handbook of chemical property estimation methods: environmental behavior of organic compounds. American Chemical Society

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Sigma-Aldrich. (2019). Squalane. Retrieved from: https://www.sigmaaldrich.com/catalog/substance/squalane4228111101311?lang=en&region=US

U.S. EPA. (2019). Estimation Programs Interface Suite, v 4.11. United States Environmental Protection Agency, Washington, DC, USA

[5] https://www.epa.gov/sites/production/files/2015-05/documents/05.pdf

4. Relevant Assessment History

EPA assessed the toxicological profile of squalane and added the chemical to the Safer Choice Program's Safer Chemical Ingredients List (SCIL) in May 2016 under the functional classes of emollients and skin conditioning agents. The SCIL[6] is a continuously updated list of chemicals that meet low-concern Safer Choice criteria.[7]

Internationally, EPA identified one assessment by the Canadian Government, which conducted an assessment of toxicity and exposure as part of its categorization of the Domestic Substance List and found that squalane did not meet its criteria for further attention.[8]

[6] https://www.epa.gov/saferchoice/safer-ingredients
[7] https://www.epa.gov/sites/production/files/2013-12/documents/dfe_master_criteria_safer_ingredients_v2_1.pdf
[8] https://canadachemicals.oecd.org/ChemicalDetails.aspx?ChemicalID=627B506D-7E94-4702-BE15-A1D73E744CFF

5. Conditions of Use

Per TSCA section 3(4), the term "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. EPA assembled information on all uses of squalane (Appendix A) to inform which uses would be determined conditions of use.[9] One source of information that EPA used to help determine conditions of use is EPA's Chemical Data Reporting (CDR). The CDR rule (previously known as the Inventory Update Rule, or IUR), under TSCA section 8, requires manufacturers (including importers) to report information on the chemical substances they produce domestically or import into the U.S., generally above a reporting threshold of 25,000 lb. per site per year. CDR includes information on the manufacturing, processing, and use of chemical substances with information dating back to the mid-1980s. CDR may not provide information on other life-cycle phases such as the chemical substance's end-of-life after use in products (i.e., disposal).

Based on CDR reporting, squalane is manufactured domestically and imported. It is used in processing (incorporation into articles, and incorporation into formulations, mixtures, or products) in toiletries and cosmetics; as well as in lubricants and lubricant additives for consumer and commercial use (EPA 2017b). According to CDR, squalane is not recycled. No information on disposal is found in CDR or through EPA's Toxics Release Inventory (TRI) Program[10] because squalane is not a TRI-reportable chemical. Although reasonably available information did not specify additional types of disposal, for purposes of this prioritization designation, EPA assumed end-of-life pathways that include releases to air, wastewater, surface water, and land via solid and liquid wastes based on the conditions of use (e.g., incineration, landfill).

To supplement CDR, EPA conducted research through the publicly available databases listed in Appendix A (Table A.2) and performed additional internet searches to clarify conditions of use or identify additional occupational[11] and consumer uses. Although EPA identified uses of squalane in personal care products, the screening review covered TSCA conditions of use for the chemical substance and personal care products were not considered in EPA's assessment. Exclusions to TSCA's regulatory scope regarding "chemical substance" can be found at TSCA section 3(2). Table 3 lists the conditions of use for squalane considered for chemical substance prioritization, per TSCA section 3(4). Table 3 reflects the TSCA uses determined as conditions of use listed in Table A.3 (Appendix A).

[9] The prioritization process, including the definition of conditions of use, is explained in the *Procedures for Prioritization of Chemicals for Risk Evaluation Under the Toxic Substances Control Act* (82 FR 33753).

[10] https://www.epa.gov/toxics-release-inventory-tri-program

[11] Occupational uses include industrial and/or commercial uses

Table 3: Conditions of Use for Squalane			
Life Cycle Stage	**Category**	**Subcategory of Use**	**Source**
Manufacturing	Domestic manufacture	Domestic manufacture	Though not reported to CDR, manufacturing is assumed to be reasonably foreseen.
	Import	Import	EPA (2017b)
Processing	Processing- incorporation into formulation, mixture or reaction	Toiletries/cosmetics - Miscellaneous manufacturing	EPA (2017b)
		Lubricants and lubricant additives - All other chemical product and preparation manufacturing	
Distribution	Distribution	Distribution	EPA (2017b)
Not known or reasonably ascertainable (NKRA)	Fuels and related products	Transformer oil, Vacuum gas oil	NLM (2018), Kirk-Othmer (2005)
Industrial/commercial/consumer uses	Paints and coatings	Paints and coatings	Reported to the ECHA database (2018)
	Cleaning and furnishing care products	Cleaning and washing products	Reported to the ECHA database (2018)
	Laboratory chemicals	Laboratory chemicals	NLM (2018a); Sigma Aldrich (2018); Reported to the ECHA database (2018); SPIN (2018)
Consumer/commercial	Tool sets		CPCat (2019)
	Veterinary products	Pet care products	DeLima Associates (2014)
Disposal	Releases to air, wastewater, solid and liquid wastes		Though not explicitly identified, releases from disposal were assumed to be reasonably foreseen [12]

[12]See Section 5 for a discussion on why releases were assumed to be reasonably foreseen for purposes of this prioritization designation.

6. Hazard Characterization

EPA reviewed peer-reviewed literature and other data sources to identify reasonably available information. This literature review approach[13] is tailored to capture the reasonably available information associated with low-hazard chemicals. EPA also used this process to verify the reasonably available information for reliability, completeness, and consistency. EPA reviewed the reasonably available information to identify relevant, quality studies to evaluate the hazard potential for squalane against the endpoints listed below. EPA's New Chemicals Program has used these endpoints for decades to evaluate chemical substances under TSCA[14] and EPA toxicologists rely on these endpoints as key indicators of potential human health and environmental effects. These endpoints also align with internationally accepted hazard characterization criteria, such as the Globally Harmonized System of Classification and Labelling of Chemicals[15] as noted above in Section 4 and form the basis of the comparative hazard assessment of chemicals.

Human health endpoints evaluated: Acute mammalian toxicity, repeated dose toxicity, carcinogenicity, mutagenicity/genotoxicity, reproductive and developmental toxicity, neurotoxicity, skin sensitization, respiratory sensitization, immunotoxicity and eye and skin irritation.

Environmental fate and effects endpoints evaluated: Aquatic toxicity, environmental persistence, and bioaccumulation and bioconcentration.

The low-concern criteria used to evaluate both human health and environmental fate and effects are included in Table 4 below.

Table 4: Low concern Criteria for Human Health and Environmental Fate and Effects

Human Health				
Acute Mammalian Toxicity[16]	**Very High**	**High**	**Moderate**	**Low**
Oral LD50 (mg/kg)	≤ 50	> 50 – 300	> 300 - 2000	> 2000
Dermal LD50 (mg/kg)	≤ 200	> 200 – 1000	> 1000 - 2000	> 2000
Inhalation LC50 (vapor/gas) (mg/L)	≤ 2	> 2 – 10	> 10 - 20	> 20
Inhalation LC50 (dust/mist/fume) (mg/L)	≤ 0.5	> 0.5 - 1.0	> 1.0 - 5	> 5

[13] Discussed in the document "Approach Document for Screening Hazard Information for Low-Priority Substances Under TSCA," which can be found at https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0450-0002.

[14] https://www.epa.gov/sustainable-futures/sustainable-futures-p2-framework-manual

[15] https://www.unece.org/fileadmin/DAM/trans/danger/publi/ghs/ghs_rev07/English/ST_SG_AC10_30_Rev7e.pdf

[16] Values derived from GHS criteria (*Chapter 3.1: Acute Toxicity.* 2009, United Nations).

Table 4: Low concern Criteria for Human Health and Environmental Fate and Effects				
Repeated Dose Toxicity, Neurotoxicity, and Immunotoxicity (90-day study)[17]		**High**	**Moderate**	**Low**
Oral (mg/kg-bw/day)		< 10	10 - 100	> 100
Dermal (mg/kg-bw/day)		< 20	20 - 200	> 200
Inhalation (vapor/gas) (mg/L/6h/day)		< 0.2	0.2 - 1.0	> 1.0
Inhalation (dust/mist/fume) (mg/L/6h/day)		< 0.02	0.02 - 0.2	> 0.2
Reproductive and Developmental Toxicity[18]		**High**	**Moderate**	**Low**
Oral (mg/kg/day)		< 50	50 - 250	> 250
Dermal (mg/kg/day)		< 100	100 - 500	> 500
Inhalation (vapor, gas, mg/L/day)		< 1	1 - 2.5	> 2.5
Inhalation (dust/mist/fume, mg/L/day)		< 0.1	0.1 - 0.5	> 0.5
Mutagenicity/ Genotoxicity[19]	**Very High**	**High**	**Moderate**	**Low**
Germ cell mutagenicity	GHS Category 1A or 1B: Substances known to induce heritable mutations or to be regarded as if they induce heritable mutations in the germ cells of humans.	GHS Category 2: Substances which cause concern for humans owing to the possibility that they may induce heritable mutations in the germ cells of humans.	Evidence of mutagenicity support by positive results *in vitro* OR *in vivo* somatic cells of humans or animals	Negative for chromosomal aberrations and gene mutations, or no structural alerts.
Mutagenicity and Genotoxicity in Somatic Cells		OR Evidence of mutagenicity supported by positive results in *in vitro* AND		

[17] Values from GHS criteria for Specific Target Organ Toxicity Repeated Exposure (*Chapter 3.9: Specific Target Organ Toxicity Repeated* Exposure. 2009, United Nations).

[18] Values derived from the US EPA's Office of Pollution Prevention & Toxics criteria for HPV chemical categorizations (*Methodology for Risk-Based Prioritization Under ChAMP*), and the EU REACH criteria for Annex IV (2007).

[19] From GHS criteria (*Chapter 3.5: Germ Cells Mutagenicity.* 2009, United Nations) and supplemented with considerations for mutagenicity and genotoxicity in cells other than germs cells.

Table 4: Low concern Criteria for Human Health and Environmental Fate and Effects				
		in vivo somatic cells and/or germ cells of humans or animals.		
Carcinogenicity[20]	**Very High**	**High**	**Moderate**	**Low**
	Known or presumed human carcinogen (GHS Category 1A and 1B)	Suspected human carcinogen (GHS Category 2)	Limited or marginal evidence of carcinogenicity in animals (and inadequate[21] evidence in humans)	Negative studies or robust mechanism-based SAR
Sensitization[22]		**High**	**Moderate**	**Low**
Skin sensitization		High frequency of sensitization in humans and/or high potency in animals (GHS Category 1A)	Low to moderate frequency of sensitization in human and/or low to moderate potency in animals (GHS Category 1B)	Adequate data available and not GHS Category 1A or 1B
Respiratory sensitization		Occurrence in humans or evidence of sensitization in humans based on animal or other tests (equivalent to GHS Category 1A or 1B)	Limited evidence including the presence of structural alerts	Adequate data available indicating lack of respiratory sensitization
Irritation/ Corrosivity[23]	**Very High**	**High**	**Moderate**	**Low**
Eye Irritation/ Corrosivity	Irritation persists for >21 days or corrosive	Clearing in 8-21 days, severely irritating	Clearing in 7 days or less, moderately irritating	Clearing in less than 24 hours, mildly irritating
Skin Irritation/ Corrosivity	Corrosive	Severe irritation at 72 hours	Moderate irritation at 72 hours	Mild or slight irritation at 72 hours

[20] Criteria mirror classification approach used by the IARC (*Preamble to the IARC Monographs: B. Scientific Review and Evaluation: 6. Evaluation and rationale.* 2006*)* and incorporate GHS classification scheme (*Chapter 3.6: Carcinogenicity.* 2009, United Nations).

[21] EPA's approach to determining the adequacy of information is discussed in the document "Approach Document for Screening Hazard Information for Low-Priority Substances Under TSCA", also released at proposal.

[22] Incorporates GHS criteria (*Chapter 3.4: Respiratory or Skin Sensitization.* 2009, United Nations).

[23] Criteria derived from the Office of Pesticide Programs Acute Toxicity Categories (US EPA. *Label Review Manual.* 2010).

Table 4: Low concern Criteria for Human Health and Environmental Fate and Effects			
Environmental Fate and Effects			
Acute Aquatic Toxicity Value (L/E/IC50)[24]	**Chronic Aquatic Toxicity Value (L/E/IC50)[24]**	**Persistence (Measured in terms of level of biodegradation)[25]**	**Bioaccumulation Potential[26]**
May be low concern if ≤10 ppm…	…and ≤1 ppm…	…and the chemical meets the 10-day window as measured in a ready biodegradation test…	…and BCF/BAF < 1000.
Low concern if >10 ppm and <100 ppm…	…and >1 ppm and <10 ppm…	…and the chemical reaches the pass level within 28 days as measured in a ready biodegradation test	
Low concern if ≥100 ppm…	…and ≥ 10 ppm…	… and the chemical has a half-life < 60 days…	

6.1 Human Health Hazard

6.1.1 Absorption, Distribution, Metabolism, Excretion

To review absorption, distribution, metabolism and excretion (ADME) endpoints without adequate quality[27] experimental data, EPA used widely accepted new approach methodologies (NAMs), such as modeling and estimation tools often based on physical-chemical properties, which provided information sufficient to fill these endpoints.

Absorption

Based on squalane's low water solubility and molecular weight (Section 3), squalane is expected to have minimal absorption from the gastrointestinal (GI) tract following oral exposure. In a study where rats were orally administered squalane, the chemical was not detected in lymph, bile, or urine samples 5, 8, and 72 hrs after exposure and 96-100% of the administered dose was excreted via feces (CIR Expert Panel, 1982; Albro and Fishbein, 1970). These results further suggest that squalane is not readily absorbed from the GI tract.

Following dermal exposure, percutaneous absorption of squalane was described as slight (low penetration) (CIR Expert Panel, 1982) based on a single study describing the application of radiolabeled squalane to normal and denuded skin of mice for 60 or 120 minutes (Wepierre et al., 1968).

[24] Derived from GHS criteria (*Chapter 4.1: Hazards to the Aquatic Environment.* 2009, United Nations), EPA OPPT New Chemicals Program (*Pollution Prevention (P2) Framework,* 2005*)* and OPPT's criteria for HPV chemical categorization (*Methodology for Risk Based Prioritization Under ChAMP. 2009).*

[25] Derived from OPPT's New Chemicals Program and DfE Master Criteria, and reflects OPPT policy on PBTs (*Design for the Environment Program Master Criteria for Safer Chemicals, 2010)*.

[26] Derived from OPPT's New Chemicals Program and Arnot & Gobas (2006) [Arnot, J.A. and F.A. Gobas, *A review of bioconcentration factor (BCF) and bioaccumulation factor (BAF) assessments for organic chemicals* in aquatic organisms. Environmental Reviews, 2006. 14: p. 257-297.]

[27] The literature search and review process to determine studies of adequate quality for inclusion in the screening review is further discussed in the document "The Approach Document for Screening Hazard Information for Low-Priority Substances under TSCA." https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0450-0002

Based on squalane's low water solubility (Section 3), absorption through the lungs is predicted to be low.

Distribution

Experimental data determined to be of adequate quality[28] on squalane not reasonably available for the assessment of distribution potential. Based on the absorption, metabolism and excretion information, it is expected that squalane will not be distributed throughout the body. If ingested, it is expected to be metabolized and excreted (described further below).

Metabolism

Because quality experimental data[28] on squalane metabolite formation were limited, the Quantitative Structure-Activity Relationship (QSAR) toolbox[29] was used to run the *in vivo* rat metabolism simulator, the skin metabolism simulator, and the rat liver S9 metabolism simulator. The rat liver S9 metabolism simulator predicted primarily C30 branched primary and tertiary alcohol oxidation metabolites, the skin metabolism simulator predicted C30 branched primary alcohol oxidation metabolites, and the *in vivo* rat metabolism simulator predicted primarily C30 branched tertiary or primary diols.

Excretion

Four days following oral exposure to squalane, approximately 96% to 100% of the administered dose was excreted via feces in rats. No detectable amounts of squalane were in the lymph, bile, or urine samples collected 5, 8, and 72 post exposure (CIR Expert Panel, 1982; Albro and Fishbein, 1970). These results indicate that following ingestion, squalane will be excreted via feces.

6.1.2 Acute Toxicity

EPA assessed the potential for mammalian toxicity from acute exposures to squalane using the results of a study following the Method Guideline for Toxicity issued by the Ministry of Health and Welfare of Japan. Rats exposed by oral gavage to 2000 mg/kg of squalane displayed no mortalities (Reported to the ECHA database, 1995a). Another oral gavage study in rats exposed to squalane also reported no mortalities at the tested dose of 1620 mg/kg (Reported to the ECHA database, 1996). An oral study in mice reported no mortalities at any dose, including the highest dose of 40,500 mg/kg (CIR Expert Panel, 1982). These results provide sufficient information to indicate low concern for acute toxicity with LD_{50}s greater than the low-concern benchmark of 2000 mg/kg.

6.1.3 Repeated Dose Toxicity

EPA assessed the potential for mammalian toxicity from repeated exposures by squalane using a combined repeated dose, reproductive, and developmental study (Reported to the ECHA database, 2013e). Rats were exposed to squalane via oral gavage. Males were treated two weeks prior to mating, for a total of 28 days, and females were treated two weeks prior to mating through postpartum day 4 for a total of 28 days. The no observed adverse effect level (NOAEL) was the highest dose tested, 1000 mg/kg-day. This result provides sufficient information to indicate low concern for

[28] The literature search and review process to determine studies of adequate quality for inclusion in the screening review is further discussed in the document "The Approach Document for Screening Hazard Information for Low-Priority Substances under TSCA." https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0450-0002.

[29] https://www.oecd.org/chemicalsafety/risk-assessment/oecd-qsar-toolbox.htm

toxicity resulting from repeated exposures by exceeding the oral low-concern benchmark of 300 mg/kg-day for a 28-day study (extrapolated from 100 mg/kg-day for a 90-day study).

6.1.4 Reproductive and Developmental Toxicity

EPA assessed the potential for reproductive and developmental toxicity using the same combined repeated dose, reproductive, and developmental study discussed above. Rats were exposed to squalane by oral gavage for 28 days (Reported to the ECHA database, 2013e). Males were treated two weeks prior to mating and females were treated two weeks prior to mating through postpartum day 4. No reproductive (mating, fertility, and estrus cycle) or developmental effects (external examinations of the pups and pup body weight gain) were observed at the highest dose tested (1000 mg/kg-day). The NOAEL for this study was 1000 mg/kg-day for both reproductive and developmental toxicity. These results provide sufficient information to indicate low concern for developmental and reproductive toxicity by exceeding the 250 mg/kg-day benchmark.

6.1.5 Genotoxicity

EPA assessed experimental gene mutation and chromosomal aberration studies as indicators of squalane's potential to cause genotoxicity. An *in vitro* gene mutation study using a mouse lymphoma cell line exposed to squalane reported negative results with and without activation (Reported to the ECHA database, 2013a). Four studies in two bacteria species, *S. typhimurium* and *E. coli*, exposed to squalane reported negative results with and without metabolic activation (Reported to the ECHA database, 2011b, 2005). Further, human lymphocytes exposed to squalane did not cause chromosomal aberrations with and without metabolic activation (Reported to the ECHA database, 2013b). These negative results in a range of species provide sufficient information to indicate low concern for squalane to cause genotoxicity.

6.1.6 Carcinogenicity

Experimental data determined to be of adequate quality[30] on squalane were not reasonably available for the assessment of carcinogenicity potential. EPA used widely accepted NAMs, such as publicly available quantitative structure activity relationship (QSAR) models and structural alerts (SA) to assess the carcinogenic potential for squalane, discussed further below.

Structural alerts represent molecular functional groups or substructures that are known to be linked to the carcinogenic activity of chemicals. The most common structural alerts are those for electrophiles (either direct acting or following activation). Modulating factors that will impact the carcinogenic potential of a given electrophile will include its relative hardness or softness, its molecular flexibility or rigidity, and the balance between its reactivity and stability.[31] For squalane and its metabolites, there is an absence of the types of reactive structural features that are present in genotoxic

[30] The literature search and review process to determine studies of adequate quality for inclusion in the screening review is further discussed in the document "The Approach Document for Screening Hazard Information for Low-Priority Substances under TSCA." https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0450-0002

[31] "Fundamental and Guiding Principles for (Q)SAR Analysis of Chemical Carcinogens with Mechanistic Considerations: Series on Testing and Assessment, No. 229." 2015. Environment Directorate, Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology.

carcinogens. Squalane is not an electrophile. ISS profiler, a QSAR model,[32] did not identify any structural alerts for squalane or its metabolites (see Figure 9 metabolic tree in Metabolic Pathway Trees Supplemental Document[33]). Further, the Virtual models for property Evaluation of chemicals within a Global Architecture (VEGA) models'[34] results indicate squalane has low potential to be carcinogenic or mutagenic with moderate reliability.

Applying expert scientific judgement based on the reasonably available information and weight of the scientific evidence, EPA finds that squalane's limited absorption, transformation profile, a lack of structural alerts, and experimental genotoxicity results provide sufficient information to indicate this chemical is unlikely to be carcinogenic or mutagenic.

6.1.7 Neurotoxicity

EPA assessed the potential for neurotoxicity from exposure to squalane on a subset of the exposed rats from the OECD Guideline 422 study described in Sections 6.1.3 and 6.1.4 used for neurotoxicity assessments. In the combined repeated dose, reproductive, and developmental study, rats were exposed to squalane by oral gavage for 28 days and neurotoxicity endpoints were observed in both adults and pups (Reported to the ECHA database, 2013e). The authors reported that males at 300 and 1000 mg/kg-day exhibited slightly lower locomotor activity than controls, but these differences were reported to not be statistically significant. Grip strength, sensory reactivity, and behavior were reported to be equivalent across all groups. Pups were evaluated for postural reflexes and no effects were observed. Based on these results, EPA determined the NOAEL to be 1000 mg/kg-day for neurotoxicity. These results provide sufficient information to indicate squalane is of low concern of neurotoxicity by exceeding the low-concern benchmark of 300 mg/kg-day (extrapolated from 100 mg/kg-day for a 90-day study).

6.1.8 Skin Sensitization

EPA assessed the potential for squalane to act as a skin sensitizing agent using three studies in humans (Reported to the ECHA database, 2012c,d, 1994b). All of these studies reported negative results for squalane, providing sufficient information to indicate low concern for skin sensitization.

6.1.9 Respiratory Sensitization

Experimental data determined to be of adequate quality[35] on squalane were not reasonably available for the assessment of respiratory sensitization potential. To model respiratory sensitization for squalane, EPA used NAMs, such as the QSAR Toolbox, version 4.2 models[36] for keratinocyte gene expression; protein binding potency h-CLAT; protein binding potency cysteine; protein binding potency lysine; and respiratory sensitization. No structural alerts were identified for squalene. The

[32] Carcinogenicity alerts by ISS 2.4 profiler as encoded in the QSAR Toolbox 4.3 (qsartoolbox.org). A summary of the results from these models is provided in Appendix B.

[33] The metabolic tree was generated using the in vivo rat metabolism simulator (v07.12) within TIMES V2.29.1.88.

[34] There are four carcinogenicity models housed within the VEGA 1.1.4 software tool available from https://www.vegahub.eu. A summary of the results from these models is provided in Appendix B.

[35] The literature search and review process to determine studies of adequate quality for inclusion in the screening review is further discussed in the document "Approach Document for Screening Hazard Information for Low-Priority Substances under TSCA." https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0450-0002.

[36] The OECD QSAR Toolbox is one of EPA's listed new approach methodologies under TSCA 4(h)(2), available at https://www.epa.gov/sites/production/files/2019-12/documents/alternative_testing_nams_list_first_update_final.pdf

weight of scientific evidence provides sufficient information to indicate low concern for respiratory sensitization.

6.1.10 Immunotoxicity

EPA reviewed the literature for immunotoxicity endpoints such as lymphoid organ weight, histopathology, and immune function. Specific endpoints included immune system function (e.g., T-cell dependent antibody response), immunophenotyping (e.g., changes in cell types), natural killer cell activity, host resistance assays, macrophage neutrophil function, and cell-mediated immunity assays. Experimental data determined to be of adequate quality[37] on squalane were not reasonably available for the assessment of immunotoxicity potential.

Repeated dose testing is designed to be comprehensive in nature and is intended to address a wide range of possible impacts, including, but not limited to immunotoxicity. The testing required to address repeated dose toxicity typically includes routine clinical observations, hematology and clinical biochemistry, body weight/food and water consumption, as well as both gross necropsy and histopathology involving organs and organ systems. For example, repeated dose studies can evaluate changes to the spleen or thymus, which with accompanying histological changes or changes in hematological parameters can indicate potential for immunological toxicity. Where immune system-related endpoints were measured in repeated dose studies, any adverse effects would be incorporated into the lowest observed adverse effect level used against the low-concern benchmarks. Therefore, EPA relied on this information from repeated dose studies when it was reasonably available. For squalane, the included repeated dose studies did not report changes in lymphoid organ weights (thymus, spleen, lymph nodes), with accompanying histopathology, or hematological changes due to exposure to this chemical substance in mammals. These results provide sufficient information to indicate low concern for immunotoxicity potential from squalane.

6.1.11 Skin Irritation

EPA assessed the potential for squalane to act as a skin irritant using four studies in humans (Reported to the ECHA database, 2012b, c, 1995b, 1994a), which all reported negative results. Two studies in rabbits (Reported to the ECHA database, 2010; CIR Expert Panel, 1982) also reported negative results for squalane acting as a skin irritant. These negative results provide sufficient information to indicate low concern for squalane to cause skin irritation.

6.1.12 Eye Irritation

Experimental data determined to be of adequate quality[38] on squalane were not reasonably available for the assessment of eye irritation. Given the endogenous nature of this chemical and overall low-hazard profile, including negative results for skin sensitization and skin irritation, EPA has sufficient information to anticipate low concern for eye irritation.

[37] The literature search and review process to determine studies of adequate quality for inclusion in the screening review is further discussed in the document "Approach Document for Screening Hazard Information for Low-Priority Substances under TSCA." https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0450-0002.

[38] The literature search and review process to determine studies of adequate quality for inclusion in the screening review is further discussed in the document "Approach Document for Screening Hazard Information for Low-Priority Substances under TSCA." https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0450-0002.

6.1.13 Hazards to Potentially Exposed or Susceptible Subpopulations

The above information supports a low human health hazard finding for squalane based on low-concern criteria. This finding includes considerations such as the potential for developmental toxicity, reproductive toxicity, and acute or repeated dose toxicity that may impact potentially exposed or susceptible subpopulations. Based on the hazard information discussed in Section 6, EPA did not identify populations with greater susceptibility to squalane.

6.2 Environmental Hazard

EPA estimated environmental hazard of squalane using experimental acute aquatic toxicity data and applying acute-to chronic ratios to predict chronic toxicity. Because of the low water solubility and high log K_{ow} values (see Table 2), EPA determined that squalane is outside the applicability domain of the ECOSAR model to predict acute or chronic aquatic toxicity. Typically, when a reliable experimental value for K_{ow} is unavailable, EPA estimates the log K_{ow} using the KOWWIN™ program. The modeled K_{ow} from KOWWIN™ is the default value used in the ECOSAR model. However, predictions for substances with an estimated log $K_{ow} > 9$ by KOWWIN™ have increased uncertainty because the KOWWIN™ training set does not contain chemicals with a log $K_{ow} > 8$ and the validation set does not contain any chemicals with a log $K_{ow} > 11$.

6.2.1 Acute Aquatic Toxicity

Aquatic vertebrates acutely exposed to squalane for 96 hours reported an LC_{50} greater than the highest dose tested, 3.9E-3 mg/L (measured concentration) (Reported to the ECHA database, 2013d). Aquatic invertebrates exposed to squalane for 48 hours reported no mortality at the highest dose tested, 3.8E-3 mg/L (measured concentration) (Reported to the ECHA database, 2013c). The highest doses tested for these two trophic levels exceed the water solubility of squalane and demonstrated no adverse effects. Since the tested doses exceed the water solubility, the dissolved (and bioavailable) concentration of the chemical in the water column will be limited to the point that acute toxicity is unlikely to be exhibited. EPA also predicts no effects at saturation for algae given the low-hazard findings for vertebrates and invertebrates and low water solubility of squalane. These results provide sufficient information to indicate squalane is low concern for acute exposures to the aquatic environment.

6.2.2 Chronic Aquatic Toxicity

Because the structure of squalane is beyond the domain of EPISuite and ECOSAR, EPA relied on an acute-to-chronic ratio to predict chronic aquatic toxicity for vertebrates and invertebrates using Sustainable Futures methodologies.[39] For neutral organics, such as squalane, chronic toxicity values are predicted for vertebrates and invertebrates by applying a factor of 10 to the acute aquatic toxicity values. In this case, the vertebrate and invertebrate chronic toxicity values are expected to be greater than 3.9E-4 mg/L, which exceeds the water solubility of squalane, limiting the dissolved (and bioavailable) concentration of the chemical in the water column to the point that chronic toxicity is unlikely to be exhibited. A similar finding is expected for algae, given squalane's low water solubility and that the neutral organic acute-to-chronic ratio is calculated by applying a factor of 4 for algae.

[39] https://www.epa.gov/sites/production/files/2015-05/documents/06.pdf

Additionally, biodegradation is expected to further reduce the dissolved concentration in the environment. These results provide sufficient information to indicate squalane is low concern for chronic exposures to the aquatic environment.

6.3 Persistence and Bioaccumulation Potential

6.3.1 Persistence

EPA assessed environmental persistence for squalane using two experimental studies following OECD Guideline 301 B. One study demonstrated squalane was inherently biodegradable under aerobic conditions and degraded by more than 67% on day 29 (Reported to the ECHA database, 2011a). The other study reported squalane as readily biodegradable under aerobic conditions and degraded more than 73% by day 28 and met the 10-day window (Reported to the ECHA database, 2012a). No degradation products of concern were identified for this chemical substance. These results provide sufficient information to indicate low concern for persistence based on the low-concern benchmark of a half-life less than 60 days with no degradation products of concern and indicate this chemical will have low persistence.

Anaerobic biodegradation data were not available for squalane. Squalane is an aliphatic alkane, which can degrade under sulfate-reducing conditions via fumarate addition by alkylsuccinate synthase, followed by rearrangement of the C-skeleton, then decarboxylation, and beta-oxidation yielding acetate (Ghattas et al. 2017[40]). While EPA cannot be certain of the rate at which this anerobic pathway may occur, this information supports the potential for squalane to anaerobically biodegrade. In addition, given the chemical has limited water solubility and is expected to adsorb to sediments and soil, EPA has sufficient information to anticipate low concern for this chemical in anaerobic environments.

6.3.2 Bioaccumulation Potential

To address the potential for squalane to bioaccumulate, EPA calculated biomagnification factors (BMFs) based on a 10-month absorption, retention, and depuration study using Rainbow trout (Cravedi and Tulliez, 1986)). This study reported 38% of squalane was absorbed through the intestines during the uptake phase. Neither a bioconcentration factor nor a bioaccumulation factor can be directly determined from this study because the chemical is dosed only in feed and not in the water phase. In addition, bioaccumulation factors are generally based on environmental data and not laboratory data.

The data provided in the study can be used to calculate a biomagnification factor (BMF), which represents the ratio of the chemical concentration in the organism and the concentration in its diet (prey). Biomagnification is an indicator of the increase of squalane in a food web, with BMF values greater than one indicating increased accumulation in higher trophic levels of a food web. The study does not use a constant feeding rate as recommended by the current OECD Guideline 305 and the body mass of the fish increases rapidly, particularly at the end of the study, so it is unlikely that a steady state has been reached. Therefore, EPA determined that a kinetic BMF, in addition to a kinetic

[40] Ghattas, A.K., Fischer, F., Wick, A., and Ternes, T. (2017) Anaerobic biodegradation of (emerging) organic contaminants in the aquatic environment. *Water Research*, 116 (1): 268-295. Available at: https://www.sciencedirect.com/science/article/pii/S0043135417300763.

BMF adjusted for growth dilution, were the appropriate calculations to apply to this study. The OECD Guideline 305 for dietary studies recommends calculating the kinetic BMF based on the depuration of the chemical while the fish are given non-contaminated feed.

Although this study was completed prior to the harmonization of BMF studies and therefore did not follow OECD Guideline 305, EPA applied the method outlined in annex 7 of the OECD Guideline 305 document to calculate kinetic BMFs based on the best available data. From the information in the study, EPA calculated a kinetic BMF of 0.059 (BMF_k) based on the uptake rate for the first week and a growth-adjusted kinetic BMF of 0.12 (BMF_{kg}).[41] To help interpret these values, BMF values much lower than 1 indicate biomagnification is not likely to occur.[42] These results indicate squalane is not likely to biomagnify in the food chain.

Further, as noted in Section 2, squalane is an endogenous substance found in human sebum. It is the fully hydrogenated derivative of squalene, also an endogenous substance. Squalene is also found in shark liver oil and other natural oils.

Based on the reasonably available information on this substance and weight of scientific evidence including the endogenous nature of this chemical, excretion in mammals and low experimental biomagnification factor in fish, EPA has sufficient information to find there is low potential and minimal concern for bioaccumulation of squalane.

[41] The depuration rate is 0.0079/day (k_2), the growth rate during depuration is 0.0041/day (k_g) and the weight adjusted depuration rate (k_{2g}) is 0.0038/day. All variable names are based on OECD Guideline 305 (see tables in Appendix B for full calculation details).

[42] US EPA 2009; KABAM Version 1.0 User's Guide and Technical Documentation - Appendix F -Description of Equations Used to Calculate the BCF, BAF, BMF, and BSAF Values. Available from, as of November 20, 2019: https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/kabam-version-10-users-guide-and-technical-3.

7. Exposure Characterization

EPA considered reasonably available information on exposure for squalane. In general, there is limited information on exposure for low-hazard chemicals. EPA identified sources of information relevant to squalane's exposure potential, which included the CDR database and other databases and public sources. Of these sources, the CDR database was the primary source of information on the conditions of use for this exposure characterization. EPA also consulted sources of use information from other databases and public sources (listed in Table A.2). EPA used these sources only where they augmented information from the CDR database to inform intended, known, or reasonably foreseen uses (Section 5).

As shown in Tables 3 and A.3, squalane is used in processing (incorporation into article, and incorporation into formulation, mixture, or product) in toiletries and cosmetics and lubricants and lubricant additives; as well as in paints and coatings and cleaning and furnishing care products for consumer and commercial use, for example (EPA 2017b). Non-TSCA uses, including those excluded under TSCA section 3(2), are beyond the scope of this assessment (See Table A.3).

Under the conditions of use identified in Table 3, EPA assessed the potential exposure to the following categories: the environment, the general population, and potentially exposed or susceptible subpopulations including workers and consumers.

7.1 Production Volume Information

Production volume information for squalane is based on an analysis of CDR data reported from 1986 to 2015.[43] Prior to 2006, squalane was not reported in the CDR. This does not mean it was not being produced or imported, but more likely that no single entity site was producing above the reporting threshold. In reporting year 2006, aggregate production volume for squalane was less than 500,000 lbs. According to CDR, since 2011, production volume has risen from a range of 100,000 lbs to less than 500,000 lbs. to a range of 1,000,000 lbs. to less than 10,000,000 lbs. in 2014 and 2015.

7.2 Exposures to the Environment

EPA expects most exposures to the environment to occur during the manufacturing and processing of squalane. Exposure is also possible from other uses, such as distribution, consumer, industrial, and commercial use, and disposal. These activities could result in releases of squalane to media including surface water, landfills, and air.

Given squalane's low water solubility, releases to surface water are expected to result in minimal amounts of squalane present in the water column. The log K_{oc} indicates squalane will adsorb to sediment and soil particles. Further, EPA expects high levels of removal of squalane during wastewater treatment (either directly from the facility or indirectly via discharge to a municipal treatment facility or Publicly Owned Treatment Works (POTW), see Table 2). Squalane has low persistence aerobically (discussed in Section 6.3.1) and has the potential to break down in the

[43] The CDR requires manufacturers (including importers) to report information on the chemical substances they produce domestically or import into the U.S. generally above 25,000 lb. per site per year.

environment to carbon dioxide and water. Therefore, any release of the chemical to sediments or soils in aerobic conditions will break down, reducing exposures to soil-dwelling and benthic organisms.

If disposed of in a landfill, this chemical is expected to degrade under aerobic conditions (discussed in Section 6.3.1).

If incineration releases during manufacturing and processing occur, EPA expects significant degradation of squalane to the point that it will not be present in air.

7.3 Exposures to the General Population

EPA expects the general population is unlikely to be exposed to squalane from the potential environmental releases described above. The general population is unlikely to be exposed through inhalation of ambient air because it has a low vapor pressure and will break down if incinerated. Squalane is unlikely to be present in surface water because of its low water solubility (discussed in Section 3), biodegradability (discussed in Section 6.3.1) and removal through wastewater treatment, thus reducing the potential for the general population to be exposed by oral ingestion or dermal exposure. Given the low bioaccumulation or bioconcentration potential of squalane, oral exposure to squalane via fish ingestion is unlikely.

7.4 Exposures to Potentially Exposed or Susceptible Subpopulations

EPA identified workers as a potentially exposed or susceptible subpopulation based on greater exposure to squalane than the general population during manufacturing, processing, distribution, industrial uses, and disposal. EPA also identified consumers as a population that may experience greater exposure to squalane than the general population through use of cleaning and furnishing care products, paints and coatings, and pet products, for example.

7.4.1 Exposures to Workers

Based on its reported physical form and measured melting point (Table 2), squalane is a liquid under ambient conditions. Based on squalane's conditions of use (Table 3), workers may be exposed to liquids through direct dermal contact with the substance and inhalation of aerosols if they are generated. Based on its experimental vapor pressure, squalane is not volatile at ambient temperatures, minimizing the potential for inhalation of vapors. Dermal exposures are the most likely route of exposures to workers. If dermal contact occurs, absorption of squalane through skin will be very low. Workers may be exposed to squalane in manufacturing, processing, distribution, industrial uses and disposal.

7.4.2 Exposures to Consumers

Consumers could be exposed to squalane through the use of cleaning and furnishing care products, paints and coatings, and pet care products. For all these uses, if dermal contact does occur, squalane is expected to be minimally absorbed through the skin. If the chemical is in an aerosol product and inhalation exposure occurs, absorption of squalane from the lungs is expected to be minimal. EPA does not include intentional misuse, such as people drinking products containing this chemical, as part of the known, intended or reasonably foreseen conditions of use that could lead to an exposure (82 FR 33726). Thus, oral exposures will be incidental (meaning inadvertent and low in volume). Squalane will be metabolized and excreted, further reducing the duration of exposure.

8. Summary of Findings

EPA has used reasonably available information on the following statutory and regulatory criteria and considerations to screen squalane against each of the priority designation considerations in 40 CFR 702.9(a), discussed individually in this section, under its conditions of use:

- the hazard and exposure potential of the chemical substance (See Sections 6 and 7);
- persistence and bioaccumulation (See Section 6.3);
- potentially exposed or susceptible subpopulations (See Section 7.4);
- storage near significant sources of drinking water (See Section 8.4);
- conditions of use or significant changes in the conditions of use of the chemical substance (See Section 5);
- the chemical substance's production volume or significant changes in production volume (See Section 7.1); and
- other risk-based criteria that EPA determines to be relevant to the designation of the chemical substance's priority.

EPA conducted a risk-based, screening-level review based on the criteria and other considerations above and other relevant information described in 40 CFR 702.9(c) to inform the determination of whether the substance meets the standard of a high-priority substance. High-priority substance means a chemical substance that EPA determines, without consideration of costs or other non-risk factors, may present an unreasonable risk of injury to health or the environment because of a potential hazard and a potential route of exposure under the conditions of use, including an unreasonable risk to potentially exposed or susceptible subpopulations identified as relevant by EPA (40 CFR 702.3). Designation of a low-priority substance is not a finding that the chemical substance does not present an unreasonable risk, but rather that the chemical does not meet the statutory criteria for a high-priority substance and that a risk evaluation is not warranted at the time. This section explains the basis for the final designation and how EPA applied statutory and regulatory requirements, addressed issues and reached conclusions.

8.1 Hazard and Exposure Potential of the Chemical Substance

Approach: EPA evaluated the hazard and exposure potential of squalane. EPA used this information to inform its determination of whether squalane meets the statutory criteria and considerations for final designation as a low-priority substance.

- **Hazard potential:**

For squalane's hazard potential, EPA gathered information for a broad set of human health and environmental endpoints described in detail in Section 6 of this document. EPA screened this information against low-concern benchmarks. EPA found that squalane is of low concern for human health and environmental hazard across the range of endpoints in these low-concern criteria.

- **Exposure potential:**

To understand exposure potential, EPA gathered information on physical-chemical properties, production volumes, and the types of exposures likely to be faced by workers, the general population, and consumers (discussed in Sections 3 and 7). EPA also gathered information on environmental releases. EPA identified workers, the general population, consumers, and the environment as most

likely to experience exposures. EPA determined that while the general population, consumers and workers may be exposed to squalane, exposure by dermal, inhalation and ingestion pathways are limited by squalane's physical-chemical properties. If squalane is released into the environment, its exposure potential will be minimal due to low water solubility, and further reduced through biodegradation.

Rationale: EPA determined that while workers and consumers could be exposed to squalane during processing, manufacturing, distribution, use, or disposal, these exposures do not pose a significant risk because of the chemical's low-hazard results across a range of endpoints (discussed in Section 6). In summary, the concern for exposure is mitigated by the low-hazard profile of this chemical.

Conclusion: Based on an initial analysis of reasonably available hazard and exposure information, EPA concludes that the risk-based screening-level review under 40 CFR 702.9(a)(1) does not support a finding that squalane meets the standard for a high-priority substance. The reasonably available hazard and exposure information described above provides sufficient information to support this finding.

8.2 Persistence and Bioaccumulation

Approach: EPA has evaluated both the persistence and bioaccumulation potential of squalane based on a set of EPA and internationally accepted measurement tools and benchmarks that are sound indicators of persistence and bioaccumulation potential (described in Section 6). These endpoints are key components in evaluating a chemical's persistence and bioaccumulation potential.

Rationale: EPA review of experimental data indicates squalane is readily biodegradable under aerobic conditions, with greater than 67 percent biodegradation within 28 days. EPA's calculated BMFs indicate a low potential for bioaccumulation and bioconcentration.

Conclusion: Based on an initial screen of reasonably available information on persistence and bioaccumulation, EPA concludes that the screening-level review under 40 CFR 702.9(a)(2) does not support a finding that squalane meets the standard for a high-priority substance. The reasonably available persistence and bioaccumulation information described above provides sufficient information to support this finding.

8.3 Potentially Exposed or Susceptible Subpopulations

Approach: 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 of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, consumers, or the elderly." EPA identified workers engaged in the manufacturing, processing, distribution, use, and disposal of squalane as a potentially exposed or susceptible subpopulation (described in more detail in Section 7). Consumers are also a potentially exposed subpopulation because of their use of cleaning and furnishing care products, paints and coatings, and pet care products (described in more detail in Section 7).

Rationale: EPA expects workers and consumers to have a higher exposure to squalane than the general population. Because of the low-concern hazard profile for squalane, this potential for exposure does not pose a significant increase in risk for consumers or workers.

Conclusion: Based on the Agency's understanding of the conditions of use and expected users such as potentially exposed or susceptible subpopulations, EPA concludes that the screening-level review under 40 CFR 702.9(a)(3) does not support a finding that squalane meets the standard for a high-priority substance. The conditions of use could result in increased exposures to certain populations. Even in light of this finding, the consistently low-concern hazard profile of squalane provides sufficient evidence to support a finding of low concern. The reasonably available information on conditions of use, hazard, and exposure described above provides sufficient information to support this finding.

8.4 Storage near Significant Sources of Drinking Water

Approach: In Sections 6 and 7, EPA explains its evaluation of the elements of risk relevant to the storage of squalane near significant sources of drinking water. For this criterion, EPA focused primarily on the chemical substance's potential human health hazards, including to potentially exposed or susceptible subpopulations, and environmental fate properties, and explored a scenario of a release to a drinking water source. EPA also investigated whether the chemical was monitored for and detected in a range of environmental media. This requirement to consider storage near significant sources of drinking water is unique to prioritization under TSCA Section 6(b)(1)(A) and 40 CFR 702.9(a)(4).

Rationale: In terms of health hazards, squalane is expected to present low concern to the general population, including potentially exposed or susceptible subpopulations, across a spectrum of health endpoints.

In the event of an accidental release into a surface drinking water source, squalane is expected to be insoluble in water (see Section 3) and has low persistence (see Section 6) in the drinking water supply. In the event of an accidental release to land, the estimated log K_{oc} indicates this substance is immobile in soil, which along with its water insolubility, shows a decreased potential to contaminate groundwater, including well water. Fate and transport evaluations indicate squalane is likely to partition into sediment, predicted to biodegrade under aerobic conditions (see Section 3), and unlikely to bioaccumulate (see Section 6), minimizing the likelihood that the chemical would pose a longer-term drinking water contamination threat.

A sudden release of large quantities of the chemical near a drinking water source could have immediate effects on the usability of a surface drinking water source. If such a release were to occur, two primary factors would operate together to reduce concern. First, the chemical would be expected to present low concern to the general population, including susceptible subpopulations, across a spectrum of health endpoints (see Section 6). Second, squalane would likely remain bound to sediments or soil and degrade in aerobic environments (see Section 6). Together, these factors mean that any exposures to this chemical through drinking water sources would be short-lived, and that if ingestion were to take place, concern for adverse health effects would be low. In addition, fate and transport evaluation indicated squalane would be unlikely to bioaccumulate (see Section 6).

EPA also explored whether the chemical had been identified as a concern under U.S. environmental statutes in the past. EPA searched lists of chemicals and confirmed that squalane does not appear on these lists. The lists reviewed include EPA's List of Lists (https://www.epa.gov/sites/production/files/2015-03/documents/list_of_lists.pdf). EPA also searched the lists of chemicals included in the National Primary Drinking Water Regulations and the Unregulated Contaminant Monitoring Rule (UCMR) under the Safe Drinking Water Act (SDWA).

Conclusion: Based on a qualitative review of a potential release near a significant source of drinking water, EPA concludes that the screening-level review of squalane under 40 CFR 702.9(a)(4) does not support a finding that squalane meets the standard for a high-priority substance. The reasonably available information on storage near significant sources of drinking water described above provides sufficient information to support these findings.

8.5 Conditions of Use or Significant Changes in Conditions of Use of the Chemical Substance

Approach: EPA evaluated the conditions of use for squalane and related potential exposures and hazards.

Rationale: EPA evaluated the conditions of use of squalane (see Section 5 and Appendix A) and found it to have a broad range of conditions of use. EPA expects that even if the conditions of use were to expand beyond activities that are currently known, intended or reasonably foreseen, the outcome of the screening review would likely not change and would not alter the Agency's conclusion of low concern. EPA bases this expectation on squalane's consistently low-concern hazard characteristics across the spectrum of hazard endpoints and regardless of a change in the nature or extent of its use and resultant increased exposures.

Conclusion: EPA's qualitative evaluation of potential risk does not support a finding that squalane meets the standard for a high-priority substance, based on its low-hazard profile under the current conditions of use. EPA concludes that even if conditions of use broaden, resulting in an increase in the frequency or amount of exposures, the analysis conducted to support the screening-level review under 40 CFR 702.9(a)(5) would not change significantly. In particular, the analysis of concern for hazard, which forms an important basis for EPA's findings, would not be impacted by a change in conditions of use. Therefore, such changes would not support a finding that squalane meets the standard for a high-priority substance. The reasonably available information on conditions of use, or significant changes in conditions of use, described above provides sufficient information to support this finding.

8.6 The Volume or Significant Changes in Volume of the Chemical Substance Manufactured or Processed

Approach: EPA evaluated the current production volumes of squalane (Section 7.1) and related potential exposures (Sections 7.2 through 7.4).

Rationale: EPA used reasonably available information on production volume (see Appendix A) in considering potential risk. It is possible that designation of squalane as a low-priority substance could result in increased use and higher production volumes. EPA expects, however, that any changes in squalane's production volume would not alter the Agency's assessment of low concern given the low-

hazard profile of the chemical. EPA bases this expectation on squalane's consistently low-concern hazard characteristics across the spectrum of hazard endpoints. This expectation would apply, even with a significant change in the volume of the chemical manufactured or processed and resultant increased exposures.

Conclusion: Based on this screening criteria under 40 CFR 702.9(a)(6), EPA concludes that even if production volumes increase, resulting in an increase in the frequency or levels of exposures, squalane does not meet the standard for a high-priority substance. The reasonably available information on production volume, or significant changes in production volume, described above provides sufficient information to support this finding.

8.7 Other Considerations

EPA did not identify other considerations for the screening review to support the final designation of squalane as a low-priority substance.

9. Final Designation

Based on a risk-based screening-level review of the chemical substance and, when applicable, relevant information received from the public and other information as appropriate and consistent with TSCA section 26(h), (i) and (j), EPA concludes that squalane does not meet the standard for a high-priority substance. The reasonably available information described above provides sufficient information to support this finding. Accordingly, EPA is designating squalane as a low-priority substance.

Appendix A: Conditions of Use Characterization

EPA gathered information on and related to conditions of use including uses of the chemical, products in which the chemical is used, types of users, and status (e.g., known, regulated).

A.1 CDR Manufacturers and Production Volume

The Chemical Data Reporting (CDR) rule (previously known as the Inventory Update Rule, or IUR), under TSCA section 8, requires manufacturers (including importers) to report information on the chemical substances they produce domestically or import into the U.S., generally above a reporting threshold of 25,000 lb. per site. According to the 2016 Chemical Data Reporting (CDR) database, two companies manufactured or imported squalane at two sites for reporting year 2015. Individual production volumes were withheld by EPA to protect against disclosure of CBI.

Table presents the historic production volume of squalane from the CDR from 1986-2015. Prior to 2006, squalane was not reported in the CDR. This does not mean it was not being produced or imported, but more likely that no single entity site was producing above the reporting threshold. In reporting year 2006, aggregate production volume for squalane was less than 500,000 lbs. According to CDR, since 2011, production volume has risen from a range of 100,000 lbs to less than 500,000 lbs.to a range of 1,000,000 lbs. to less than 10,000,000 lbs. in 2014 and 2015.

Table A.1: 1986-2015 National Production Volume Data for Squalane (Non-Confidential Production Volume in Pounds)

1986	1990	1994	1998	2002	2006	2011	2012	2013	2014	2015
NDR	NDR	NDR	NDR	NDR	<500 K	100K-<500K	100K-<500K	500 K - <1M	1M - <10M	1M - <10M

Source(s):
EPA (2018a; 2017b; 2006; 2002); Sherlock (2019)

Note(s):
K = Thousand; M = Million; NDR = No data reported

A.2 Uses

A.2.1 Methods for Uses Table

Section A.1 provides a list of known uses of squalane, organized by category of use. To compile the uses, EPA searched publicly available databases listed in Table A.2 and conducted additional internet searches to clarify uses. Search terms differed among databases because of different search term requirements for each database (i.e., some databases search by CASRN while others search by chemical name).

Table A.2: Sources Searched for Uses of Squalane

Title	Author and Year	Search Term(s)	Found Use Information? [1]
Sources searched for all use reports			
California Links to Pesticides Data	California Dept of Pesticide Regulation (2013)	111-01-3	No
Canada Chemicals Management Plan information sheets	Government of Canada (2018)	Squalane; Tetracosane	No
Chemical and Product Categories (CPCat)	Dionisio et al. (2015)	111-01-3	Yes
ChemView [2]	EPA (2018a)	111-01-3	Yes
Children's Safe Product Act Reported Data	Washington State Dept. of Ecology (2018)	111-01-3	No
Consumer Product Information Database (CPID)	DeLima Associates (2018)	111-01-3	Yes
Danish surveys on chemicals in consumer products	Danish EPA (2018)	N/A, There is no search, but report titles were checked for possible information on the chemical	Yes
Datamyne	Descartes Datamyne (2018)	Squalane	No
DrugBank	DrugBank (2018)	111-01-3	No
European Chemicals Agency (ECHA) Registration Dossier	ECHA (2018)	111-01-3	Yes
eChemPortal [2]	OECD (2018)	111-01-3	Yes
Envirofacts [2]	EPA (2018b)	111-01-3	No
Functional Use Database (FUse)	EPA (2017a)	111-01-3	Yes
Kirk-Othmer Encyclopedia of Chemical Technology	Kirk-Othmer (2006)	Squalane	Yes
Non-Confidential 2016 Chemical Data Reporting (CDR)	EPA (2017b)	111-01-3	Yes
PubChem Compound	Kim et al. (2016)	111-01-3	Yes
Safer Chemical Ingredients List (SCIL)	EPA (2018d)	111-01-3	Yes

Table A.2: Sources Searched for Uses of Squalane			
Title	**Author and Year**	**Search Term(s)**	**Found Use Information?** [1]
Synapse Information Resources [2]	Synapse Information Resources (n.d.)	Squalane; Tetracosane	No
Resource Conservation and Recovery Act (RCRA)	EPA (2018c)	Squalane; Tetracosane	No
Scorecard: The Pollution Information Site	GoodGuide (2011)	111-01-3	Yes
Skin Deep Cosmetics Database	EWG (2018)	111-01-3	Yes
Toxics Release Inventory (TRI)	EPA (2018f)	111-01-3	No
TOXNET [2]	NLM (2018b)	111-01-3	Yes
Ullmann's Encyclopedia of Industrial Chemistry	Ullmann's (2000)	Squalane; 111-01-3	No
Additional Sources Identified from Reasonably Available Information			
Sigma-Aldrich	Sigma Aldrich (2018)	Incidentally identified while researching into details of this chemical's uses and products.	Yes
Substances in Preparations in Nordic Countries (SPIN)	SPIN (2018)		
U.S. EPA InertFinder	EPA (2018e)		
U.S. Food and Drug Administration (FDA)	FDA (2018)		
Wedgewood Pharmacy	Wedgewood Pharmacy (2017)		

Note(s):

1. If use information was found in the resource, it will appear in Table A.3 unless otherwise noted.
2. This source is a group of databases; thus, the exact resource(s) it led to will be cited instead of the database as whole.

The U.S. Patent and Trademark Office has an online database that shows 6,899 patents referencing "squalane" (U.S. Patent and Trademark Office (USPTO) 2018). Although patents could be useful in determining reasonably foreseen uses, it is difficult to confirm whether any of the patented technologies are currently in use. Uses inferred from patents containing squalane were not included in Table A.3. Note that the uses in Table A.3 that are covered under TSCA are included in Section 5, Table 3 of this document.

A.2.2 Uses of Squalane

Table A.3: Uses of Squalane		
Use	**Expected Users**	**Description of Use and References**
Miscellaneous TSCA Uses		
Cleaning and washing products	Consumer, commercial, industrial	ECHA (2018) The ECHA registration dossier identifies use of squalane in moist disinfecting wipes in European countries, including for personal use and paper and board treatment. CPID identifies two old laundry products, but no current products, that contain squalane. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are based on inclusion in ECHA's consumer uses, uses by professional workers, and uses at industrial sites.
Laboratory chemicals	Commercial, industrial	EPA (2017b); NLM (2018a); Sigma Aldrich (2018); ECHA (2018); SPIN (2018) CDR reports use of squalane as a lubricant and lubricant additive in the manufacture of chemical products and preparations. Haz-Map also identifies use of squalane as a lubricant. ECHA identifies use as a laboratory reagent, chemical intermediate, lubricant, grease, release product, pH-regulator, flocculant, precipitant, neutralization agent, and extraction agent in European countries. SPIN identifies use in the manufacture of chemicals and chemical products in Nordic countries. Expected users are industrial based on CDR's Industrial Processing and Use report and professional based on ECHA's uses by professional workers.
Paints and coatings	Consumer, commercial, industrial	ECHA (2018) The ECHA registration dossier identifies use of squalane in consumer and commercial painting and industrial paints, coatings, paint thinners, and paint removers in European countries. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are based on inclusion in ECHA's consumer uses, uses by professional workers, and uses at industrial sites.

Table A.3: Uses of Squalane		
Use	**Expected Users**	**Description of Use and References**
Pesticides	Unknown	EPA (2018e); GoodGuide (2011) EPA lists squalane as an inert ingredient approved for nonfood use in the United States. GoodGuide identifies use of squalane in one miticide. The California Department of Pesticide Regulation does not list any pesticides currently used in that state that contain squalane, and the NPIRS does not list any federally active pesticide products that contain squalane. Expected users are unknown, due to the limited availability of information.
Pet care	Consumer	DeLima Associates (2014) CPID generally lists consumer products; therefore, the expected users are consumer.
Tool sets	Consumer	Dionisio et al. (2015) CPCat identifies use of squalane in tool sets. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are consumer based on CPCat's identification under retail product categories.
Transformer oil	Unknown	NLM (2018a) Haz-Map identifies use of squalane in transformer oil. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are unknown, due to the limited availability of information.
Vacuum gas oil	Unknown	Kirk-Othmer (2005) Kirk-Othmer identifies use of squalane in vacuum gas oils. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are unknown, due to the limited availability of information.

Table A.3: Uses of Squalane		
Use	**Expected Users**	**Description of Use and References**
Non-TSCA Uses		
After shave	Consumer	EWG (2018); DeLima Associates (2001a) EWG and CPID identify after shave products that contain squalane, however no products could be found that are currently for sale and it is unknown whether this is an ongoing use in the United States. EWG and CPID generally list consumer products; therefore, the expected users are consumer.
After sun product	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Anti-aging cream	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Antiperspirant/ deodorant	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Around-eye cream	Consumer	EWG (2018); DeLima Associates (2013b) EWG and CPID generally list consumer products; therefore, the expected users are consumer.
Baby lotion	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Baby soap	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Baby sunscreen	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.

Table A.3: Uses of Squalane		
Use	**Expected Users**	**Description of Use and References**
Baby vapor rub	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Beauty or blemish (BB) cream	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Blush	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Body firming lotion	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Body oil	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Bronzer/ highlighter	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Color correcting (CC) cream	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Concealer	Consumer	DeLima Associates (2013a) EWG and CPID generally list consumer products; therefore, the expected users are consumer.
Damaged skin treatment	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.

Table A.3: Uses of Squalane		
Use	**Expected Users**	**Description of Use and References**
Diaper cream	Consumer	EWG (2018) EWG identifies one diaper cream product containing squalane, however this product does not appear to be for sale, and it is unknown whether this is an ongoing use in the United States. EWG generally lists consumer products; therefore, the expected users are consumer.
Eye liner	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Eyeshadow	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Facial cleanser	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Facial moisturizer	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Facial powder	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Foot moisturizer	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Foundation	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Hair conditioner	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.

Table A.3: Uses of Squalane		
Use	**Expected Users**	**Description of Use and References**
Hair shampoo	Consumer	EWG (2018); DeLima Associates (2001c) EWG and CPID generally list consumer products; therefore, the expected users are consumer.
Hair spray	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Hair styling aide	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Hair treatment/ serum	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Hand cream	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Lip balm	Consumer	DeLima Associates (2003) EWG and CPID generally list consumer products; therefore, the expected users are consumer.
Lip balm with SPF	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Lip liner	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Lipstick	Consumer	EWG (2018); DeLima Associates (2012) EWG and CPID generally list consumer products; therefore, the expected users are consumer.
Makeup primer	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.

Table A.3: Uses of Squalane		
Use	**Expected Users**	**Description of Use and References**
Makeup remover	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Makeup with SPF	Consumer	EWG (2018); DeLima Associates (2011) EWG and CPID generally list consumer products; therefore, the expected users are consumer.
Mascara	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Mask	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Nail treatment	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Oil controller	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Perfumes	Consumer, commercial, industrial	NLM (2018a); ECHA (2018) Haz-Map identifies use of squalane as an additive for perfumes. ECHA identifies use of squalane in perfumes and fragrances in European countries, however, the International Fragrance Association (2018) does not include squalane in their list of standards. ECHA identifies use in perfumes and fragrances under consumer uses, uses by professional workers, and uses at industrial sites.

Table A.3: Uses of Squalane		
Use	**Expected Users**	**Description of Use and References**
Pharmaceuticals	Unknown	FDA (2018); NLM (2018a); ECHA (2018); Wedgewood Pharmacy (2017) FDA lists squalane as an approved inactive ingredient in oral powders and topical augmented creams, emulsion creams, and solutions. Haz-Map identifies use of squalane as drug additive, and Wedgewood Pharmacy identifies use in non-approved veterinary drugs. The ECHA registration dossier identifies use of squalane in consumer pharmaceuticals in European countries. DrugBank does not currently list any drugs that contain squalane. Expected users are unknown, due to the limited availability of information.
Serum and essences	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Shaving cream	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Skin fading/lightener	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Skin moisturizer	Consumer, industrial	EWG (2018); Danish EPA (2009); GoodGuide (2011) EWG and the Danish EPA identify use of squalane in moisturizing creams and lotions. GoodGuide identifies use of squalane as a softener in cosmetic emollient moisturizers. EWG generally lists consumer products; therefore, the expected users are consumer. GoodGuide lists softeners under industrial uses.
Skin moisturizer with SPF	Consumer	EWG (2018); DeLima Associates (2001b) EWG and CPID generally list consumer products; therefore, the expected users are consumer.
Styling gel/ lotion	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.

Table A.3: Uses of Squalane		
Use		**Description of Use and References**
Sunless tanning	Consumer	EWG (2018); DeLima Associates (2015) EWG and CPID generally list consumer products; therefore, the expected users are consumer.
Sunscreen	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Toners/astringents	Consumer	EWG (2018) EWG generally lists consumer products; therefore, the expected users are consumer.
Children's Products CDR reports did not include any uses in children's products; however, uses in baby lotion, soap, sunscreen, and vapor rub are found in this table. Additionally, the Danish EPA identifies exposure of 2 year-olds to squalane through consumer moisturizing creams and lotions (Danish EPA 2009).		
Recycling and Disposal In the 2016 CDR, both facilities reported not recycling (e.g., not recycled, remanufactured, reprocessed, or reused) squalane (EPA 2017b).		

A.3 References

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Appendix B: Hazard Characterization

Table B.1: Human Health Hazard

ADME

Source	Exposure Route	Species & strain (if available)	Duration	Study Details
4968730	Absorption, dermal	Mice	1-2 hours	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not reported • GLP not reported **Results:** • 1-hour absorption: 3.05 ± 0.94 ug/cm2, with an average rate of 0.12 nmol/cm^2/minute • 2-hour absorption: 5.25 ± 1.65 ug/cm2, with an average rate 0.103 nmol/cm^2/minute

Acute Mammalian Toxicity

Source	Exposure Route	Species & strain (if available)	Duration	Doses and replicate number	Effect	Study Details
5016720	Oral (gavage)	Sprague Dawley rats	Single dose followed by 14-day observation	**Dose:** 2000 mg/kg **Replicates:** 5 per sex	**LD_{50}** > 2000 mg/kg	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not reported • Method Guideline for Toxicity Studies issued by the Ministry of Health and Welfare of Japan (MHW) • GLP compliant
5016730	Oral (gavage)	Wistar rats	Single dose followed by 14-day observation	**Dose:** 1620 mg/kg **Replicates:** 5 per sex	**LD_{50}** > 1620 mg/kg	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not reported • Method OECD 84/449 L251 (25/04/1984) • Not GLP compliant
4968730	Oral	Mice	Single dose	**Doses:** 4050, 10125, 20250, and 40500 mg/kg **Replicates:** 10-20 per group	**LD_{50}** > 40500 mg/kg	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not reported • GLP compliance not reported

Table B.1: Human Health Hazard						
Repeated Dose Toxicity						
Source	**Exposure Route**	**Species & strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
5016708	Oral (gavage)	Wistar Hannover RccHan;WIST rats	Males were treated from 2 weeks prior to mating for a minimum of 28 days. Females were treated from 2 weeks prior to mating through postpartum day 4 (PD4)	**Doses:** 0, 100, 300, and 1000 mg/kg **Replicates:** 10 per sex per dose	**NOAEL**: 1000 mg/kg-day	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not reported • OECD Guideline 422 • GLP compliant
Reproductive Toxicity						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
5016708	Oral (gavage)	Wistar Hannover RccHan;WIST rats	Males were treated from 2 weeks prior to mating for a minimum of 28 days. Females were treated from 2 weeks prior to mating through postpartum day 4 (PD4)	**Doses:** 0, 100, 300, and 1000 mg/kg **Replicates:** 10 per sex per dose	**NOAEL**: 1000 mg/kg-day	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not reported • OECD Guideline 422 • GLP compliant

Table B.1: Human Health Hazard						
Developmental Toxicity						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
5016708	Oral (gavage)	Wistar Hannover RccHan;WIST rats	Males were treated from 2 weeks prior to mating for a minimum of 28 days. Females were treated from 2 weeks prior to mating through postpartum day 4 (PD4)	**Doses:** 0, 100, 300, and 1000 mg/kg **Replicates:** 10 per sex per dose	**NOAEL**: 1000 mg/kg-day	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not reported • OECD Guideline 422 • GLP compliant
Cancer						
Source			**Effect**			**Study Details**
Oncologic v8.0			Oncologic currently has no assessment criteria regarding diols.			**Results:** Structure could not be evaluated by Oncologic.
ISS v2.4[44]			Negative (Estimated) Squalane is a saturated hydrocarbon which does not contain any structural features indicative of electrophilic potential.			**Methods:** Carcinogenicity alerts (genotoxic and non-genotoxic) by ISS profiler as available within the OECD Toolbox v4.3 **Results:** No alerts were identified for the parent structure or its metabolites see (see Figure 9 metabolic tree in Metabolic Pathway Trees Supplemental Document[45]).

[44] Carcinogenicity alerts by ISS profiler comprises 55 structural alerts for genotoxic and non-genotoxic carcinogenicity. The alerts have been compiled upon existing knowledge of the mechanism of action of carcinogenic chemicals that have been published elsewhere (Benigni and Bossa (2011) *Chem Rev* 111: 2507-2536 and Benigni R et al. (2013) *Chem Rev.* 113: 2940-2957).

[45] The metabolic tree was generated using the in vivo rat metabolism simulator (v07.12) within TIMES V2.29.1.88.

Table B.1: Human Health Hazard						
VEGA 1.1.4[46]				Squalane was processed through all 4 models. ISS 1.0.2 predicted it to be non-carcinogenic with moderate reliability.		**Methods:** VEGA 1.1.4 contains 4 models for carcinogenicity – CAESAR 2.1.9, ISS 1.0.2, IRFMN/Antares 1.0.0, IRFMN/ISSCAN-GX 1.0.0 **Results:** • CAESAR 2.1.9: Low reliability (Squalane lies outside of the applicability domain (AD) of the model) • ISS 1.0.2: Moderate reliability (Squalane could lie outside of the AD) • IRFMN/Antares 1.0.0: Low reliability (Squalane lies outside of the AD) • IRFMN/ISSCAN-GX 1.0.0: Low reliability (Squalane lies outside of the AD)
Genotoxicity						
Source	**Test Type & endpoint**	**Species & strain (if available)**	**Metabolic activation**	**Doses and controls**	**Results**	**Study Details**
5016711	Gene mutation (*in vitro*)	Mouse Lymphoma L5178Y cells	With and without	**Doses:** 65.94-2110 µg/mL	Negative	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not reported • OECD Guideline 476 • GLP compliant
5016721	Chromosomal aberrations (*in vitro)*	Human lymphocytes	With and without	**Doses:** 0.2-5.3 µg/mL	Negative	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity: 95% • OECD Guideline 487 • GLP compliant

[46] VEGA 1.1.4 contains 4 different models to facilitate an *in silico* assessment of carcinogenicity potential. The models are summarized in Golbamaki et al. (2016) J Environ Sci and Health Part C http://dx.doi.org/10.1080/10590501.2016.1166879 as well as in documentation that is downloadable from within the VEGA tool itself (https://www.vegahub.eu/).

- CAESAR 2.1.9 is a classification model for carcinogenicity based on a neural network.
- ISS 1.0.2 is a classification model based on the ISS ruleset (as described above for the OECD Toolbox).
- IRFMN/Antares 1.0.0 and IRFMN/ISSCAN-GX 1.0.0 are classification models based on a set of rules built with SARpy software (part of the same suite of VEGA tools https://www.vegahub.eu/) extracted from the Antares and ISSCAN-CGX datasets respectively.

Table B.1: Human Health Hazard						
5016723	Gene mutation (*in vitro)*	*E. coli*	With and without	**Doses:** 50, 100, 500, 1000 and 5000 µg/plate	Negative	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not specified • OECD Guideline 471 • GLP compliant
5016723	Gene mutation (*in vitro)*	*Salmonella typhimurium* strains TA97a, TA98, TA100 and TA1535	With and without	**Doses:** 50, 100, 500, 1000 and 5000 µg/plate	Negative	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not specified • OECD Guideline 471 • GLP compliant
5016713	Gene mutation (*in vitro)*	*S. typhimurium* strains TA1535, TA1537, TA98, and TA100	With and without	**Doses:** 50, 150, 500, 1500 and 5000 µg/plate of 50 mg/mL squalane solution	Negative	**Methods** • Test substance reported as CASRN 111-01-3 • Purity not specified • OECD Guideline 471 • GLP compliant
5016713	Gene mutation (*in vitro)*	*E. coli* strain WP2	With and without	**Doses:** 50, 150, 500, 1500 and 5000 µg/plate of 50 mg/mL squalane solution	Negative	**Methods** • Test substance reported as CASRN 111-01-3 • Purity not specified • OECD Guideline 471 • GLP compliant
Neurotoxicity						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
5016708	Oral (gavage)	Wistar Hannover RccHan;WIST rats	Males were treated from 2 weeks prior to mating for a minimum of 28 days. Females were treated from 2 weeks prior to mating through postpartum day 4 (PD4)	**Doses:** 0, 100, 300, and 1000 mg/kg **Replicates:** 10 per sex per dose	**NOAEL**: 1000 mg/kg-day	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not reported • OECD Guideline 422 • GLP compliant

Table B.1: Human Health Hazard						
Sensitization						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
5016709, 5016719	Skin	Humans	24 hours under occlusive conditions 4 times/week for 3 weeks.	**Dose:**100% undiluted squalane **Replicates:** 110 total, 55 per sex	Negative	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not reported • Not GLP compliant
5016702	Skin	Humans	24 hours	**Dose:** 100% undiluted squalane **Replicates:** 44 total, 26 females, 18 males	Negative	**Methods** • Test substance reported as CASRN 111-01-3 • Purity not reported • Not GLP compliant
Irritation						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses**	**Effect**	**Study Details**
5016715	Skin	Humans	48 hours	**Dose:** 5% squalane **Replicates:** 10 females	Negative	**Methods:** • Test substance reported as CASRN 111-01-3. • Purity not reported • Not GLP compliant
5016719	Skin	Humans	24 hours under occlusive conditions 4 times/week for 3 weeks	**Dose:** 100% undiluted squalane **Replicates:** 110 total, 55 per sex	Negative	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not reported • Not GLP compliant
5016700	Skin	New Zealand White rabbits	72 hours	**Dose:** 0.5 mL undiluted squalane **Replicates:** 3 males	Negative	**Methods** • Test substance reported as CASRN 111-01-3 • Purity not specified • Test method: EPA OPPTS 870.2500 • GLP compliant
5016710	Skin	Humans	7 days	**Doses:** 50, 75, and 100% squalane **Replicates:** 10 volunteers	Negative	**Methods** • Test substance reported as CASRN 111-01-3 • Purity not reported • Not GLP compliant

Table B.1: Human Health Hazard						
4968730	Skin	Rabbits	24 hours	**Dose:** 0.5 mL undiluted squalane	Negative	**Methods** • Test substance reported as CASRN 111-01-3 • Purity not reported • Not GLP compliant
5016703	Dermal Patch	Humans	24-hour exposure, 48-hour observation	**Dose:** unspecified **Replicates:** 10 volunteers	Negative	**Methods** • Test substance reported as CASRN 111-01-3 • Purity not reported • Not GLP compliant

Table B.2: Environmental Hazard					
Aquatic Toxicity: Experimental					
Source	**Species & strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
5016729	*Danio rerio*	96 hours	**Dose:** 100 mg/L (nominal), 3.9 µg/L measured	**LC_{50}** > 100 mg/L (nominal)	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not reported • GLP compliant **Results:** • Substance was concluded to have no effects at saturation (NES)
5016717	*Daphnia magna*	48 hours	**Dose:**100 mg/L (nominal), 3.9 µg/L measured	**LC_0** > 100 mg/L (nominal)	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not reported • OECD Guideline 202 • GLP compliant **Results:** • No immobilization observed • Substance was concluded to have no effects at saturation (NES)
Aquatic Toxicity: Estimated					
Model	Species	Predicted Effect Level	Notes		
ECOSAR v2.0 (Class: Neutral Organics)	Freshwater fish	96-hour **LC_{50}**: 1.6E-09 mg/L	**NES.** LC50 exceeds the estimated water solubility for this substance (3.2E-10 mg/L). Estimated Log K_{ow} exceeds the endpoint specific cutoff		
ECOSAR v2.0 (Class: Neutral Organics)	Daphnia magna	96-hour **EC_{50}**: 2.9E-09 mg/L	**NES.** LC50 exceeds the estimated water solubility for this substance (3.2E-10 mg/L). The estimated log K_{ow} for this chemical is greater than the endpoint specific cut-off		
ECOSAR v2.0 (Class: Neutral Organics)	Green Algae	96-hour **EC_{50}**: 2.6E-07 mg/L	**NES.**EC50 exceeds the estimated water solubility for this substance (3.2E-10 mg/L). The estimated log K_{ow} for this chemical is greater than the endpoint specific cut-off		
ECOSAR v2.0 (Class: Neutral Organics)	Green Algae	ChV: 9.3E-07 mg/L	**NES.** ChV exceeds the estimated water solubility for this substance (3.2E-10 mg/L). The estimated Log K_{ow} for this chemical is greater than the endpoint specific cut-off		

Table B.2: Environmental Hazard			
ECOSAR v2.0 (Class: Neutral Organics)	Daphnia magna	ChV: 7.2E-09 mg/L	**NES.** ChV exceeds the estimated water solubility for this substance (3.2E-10 mg/L). The estimated log K_{ow} for this chemical is greater than the endpoint specific cut-off
ECOSAR v2.0 (Class: Neutral Organics)	Freshwater fish	ChV: 6.1E-10 mg/L	**NES.** ChV exceeds the estimated water solubility for this substance (3.2E-10 mg/L). The estimated log K_{ow} for this chemical is greater than the endpoint specific cut-off

Table B.3: Fate					
Environmental Fate: Experimental					
Source	**Endpoint**	**Duration**	**Doses and number of replicates**	**Results**	**Study Details**
5016725	Biodegradation, CO2 evolution	28 days	**Dose**: not specified	• Inherently biodegradable • 10-day window was not met	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not specified • OECD 301B • GLP compliant **Results:** • 64.7% in 28 days
5016724	Biodegradation, CO2 evolution	28 days	**Dose:** 27.9 mg/L **Replicates:** 3	• Readily biodegradable • 10-day window met	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not specified • OECD 301B • Not GLP compliant **Results:** • 77% in 28 days
1525453	Photooxidation	Not specified	Not specified	Photo-oxidizes with nitrogen oxides	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not reported • GLP compliance not reported • Measured using pure squalane aerosols with average particle sizes of 103 nm, at 298K (ca. 20°C) and 1 atm, in the absence of oxygen **Results:**

Table B.3: Fate					
Environmental Fate: Experimental					
					• Reactive uptake coefficient for the combined reaction of N_2O_5 and NO_3 when NO_3 dominates the oxidation (NO_3 + aerosol) = 7.8E-03 • Reactive uptake coefficient for the combined reaction of N_2O_5 and NO_3 when N_2O_5 dominates the oxidation (N_2O_5+aerosol) = 6.2±0.9E-05

2369609	Photooxidation	Not specified	Not specified	Photo-oxidizes with hydroxyl radicals	**Methods:**
					• Test substance reported as CASRN 111-01-3
					• Purity not reported
					• GLP compliance not reported
					• Atmospheric pressure flow tube experiment was used to evaluate hydroxyl-initiated heterogeneous oxidation of pure squalane aerosols and α-pinene+O_3 secondary organic coated squalane aerosols
					Results:
					• Pure squalane aerosols (average particle size 134 nm):
					  ○ Average reactive uptake coefficient = 0.25±0.05 (0.28±0.06 after diffusion correction)
					  ○ Effective reaction rate coefficient = 1.0E-12 cm^3 /molecule-sec
					• Coated squalane aerosols (average particle size 169 nm):
					  ○ Average reactive uptake coefficient = 0.45 to 2.9
					  ○ Effective reaction rate coefficient = 3.5-E-12 cm^3 /molecule-sec

2464268	Photooxidation	Not specified	Not specified	Photo-oxidizes with hydroxyl radicals	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not reported • GLP compliance not reported • Flow tube experiment used to evaluate hydroxyl initiated heterogeneous oxidation of squalane aerosols (mean surface-weighted diameters of 164 nm) **Results:** • Hydroxyl radical decay rate constant = 1.6±0.4E-12 cm^3/ molecule-sec • Uptake coefficient = 0.36±0.11

Table B.3: Fate					
Environmental Fate: Experimental					
					• First generation byproduct (by MS): squalane-11-one; both squalanone and squalanol isomers were isolated as byproducts • EPA calculated a half-life of 6.7 days based on this study

2576167	Photooxidation	Not specified	Not specified	Photo-oxidizes with chlorine	**Methods:**
					• Test substance reported as CASRN 111-01-3
					• Purity not reported
					• GLP compliance not reported
					• Atmospheric photochemical aerosol flow tube experiment used to evaluate heterogeneous reactions of squalane particles with gas phase chlorine (Cl) radicals in the presence and absence of oxygen
					Results:
					• Effective uptake coefficients at <1% oxygen
					  ○ At [Cl2] of 8 ppm = 0.8
					  ○ At [Cl2] of 32.7 ppm = 3
					  ○ At [Cl] of 2.67E+09 molecule/cm^3 = 2.5
					  ○ At [Cl] of 2.2E+10 molecule/cm^3 = 1.4
					• Uptake coefficients were directly related to [Cl2] and inversely related to [Cl] due to the competitive rates of chain propagation and termination

2582128	Photooxidation	Not specified	Not specified	Photo-oxidizes with hydroxyl radicals	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not reported • GLP compliance not reported • Continuous flow experiment used to evaluate hydroxyl initiated heterogeneous oxidation of squalane aerosols (average particle diameter 220±20 nm) at atmospheric pressure and 25°C in the presence of oxygen **Results:** • Reactive uptake coefficient = 0.51±0.10 at [OH] = 6.87E+08 • Reactive uptake coefficient = 0.49 to 0.54 at [OH] of 1 to 7E+08 molecule/cm^3 • Reaction appears to accelerate at lower concentrations of hydroxyl radicals

Table B.3: Fate					
Environmental Fate: Experimental					
4968700	Photooxidation	Not specified	Not specified	Photo-oxidizes with hydroxyl radicals	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not reported • GLP compliance not reported • Model system measuring the heterogeneous reaction of OH radicals with sub-micron squalane particles (average particle diameter 160 nm) in the presence of oxygen; analysis done using a photochemical flow reactor combined with AMS particle analysis **Results:** • Reactive uptake coefficient for squalane was determined to be 0.30±0.07 at an average OH concentration of 1x10E+10 molecules/cm^3 • Significant volatilization of the reduced particle would be slow in the atmosphere; as aerosols become more oxygenated, volatilization becomes significant for organic material in the particle phase
4968663	BMF	10 months followed by a 2 month depuration period for Rainbow Trout	18.16 µg/g	BMF_K: 0.059 BMF_{kg}: 0.12	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not reported • GLP compliance not reported **Results:** • See calculations in Tables B.4-6 below
4968663	Average absorption	5 days	0.05% squalane	Average squalane absorption: 38%	**Methods:** • Test substance reported as CASRN 111-01-3 • Purity not reported • GLP compliance not reported

Table B.4: Depuration Calculations				
Depuration day	Concentration in fish (µg/g)	ln (concentration)	Mass of fish	ln (mass of fish)
0	18.16	2.90	179	5.19
30	16.5	2.80	186.1	5.23
60	11.32	2.43	228.8	5.43

Line fit= -0.0079; K_2= 0.0079; k_g= 0.0041

Legend:

Depuration day is based on depurating fish that were fed uncontaminated feed.

Line fit = Slope of the plot of the ln (natural logarithm) of the concentration in fish vs. depuration day based on equation A5.19 in OECD 305 Annex 5.

k_2 is the negative of the slope of the plot of the ln of the concentration vs. depuration day.

Mass of fish = mass on depuration day.

K_g is the slope of the ln (mass of fish) vs. depuration day.

Table B.5: Uptake calculation	
Uptake day	Concentration in fish
7	1.84
30	7.44
90	16.3
150	16.76
210	16.94
300	18.16

$I\alpha = 0.00046$

Legend:

$I\alpha$ = Concentration in fish/(uptake day*concentration in feed).

Equation A7.7 in OECD 305 Annex 7 (ideally meant for days 1 to 3, but here used for days 1 to 7).

Table B.6: BMF calculations	
BMF_k ($I\alpha/k_2$)	0.059
BMF_{kg} ($I\alpha/k_g$)	0.122

Legend: BMF_k = kinetic BMF; BMF_{kg}= growth-adjusted kinetic BMF

B.1 References

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Reported to the ECHA (European Chemicals Agency) database. (1995a). 2,6,10,15,19,23-hexamethyltetracosane: acute toxicity: oral: 002 supporting | experimental result. https://echa.europa.eu/registration-dossier/-/registered-dossier/14412/7/3/2/?documentUUID=8fe3000d-ce76-43f4-8f9f-f82b36cabcb4

Reported to the ECHA (European Chemicals Agency) database. (1995b). 2,6,10,15,19,23-hexamethyltetracosane: skin irritation/corrosion: 003 supporting | experimental result. https://echa.europa.eu/registration-dossier/-/registered-dossier/14412/7/4/2/?documentUUID=0e613835-e7a5-4762-b3e4-eba55002e4f4

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Reported to the ECHA (European Chemicals Agency) database. (2011a). 2,6,10,15,19,23-hexamethyltetracosane: biodegradation in water: screening tests: 001 key | experimental result. https://echa.europa.eu/registration-dossier/-/registered-dossier/14412/5/3/2

Reported to the ECHA (European Chemicals Agency) database. (2011b). 2,6,10,15,19,23-hexamethyltetracosane: genetic toxicity: in vitro: 002 key | experimental result. https://echa.europa.eu/registration-dossier/-/registered-dossier/14412/7/7/2/?documentUUID=e4b910bb-72b8-4f60-8cff-8b4e61e6fed7

Reported to the ECHA (European Chemicals Agency) database. (2011c). 2,6,10,15,19,23-hexamethyltetracosane: biodegradation in water: screening tests: 001 key | experimental result. https://echa.europa.eu/registration-dossier/-/registered-dossier/14412/5/3/2

Reported to the ECHA (European Chemicals Agency) database. (2012a). 2,6,10,15,19,23-hexamethyltetracosane: biodegradation in water: screening tests: 004 supporting | experimental result. https://echa.europa.eu/registration-dossier/-/registered-dossier/14412/5/3/2/?documentUUID=1f1f792c-0997-4f6d-afc3-f90103cab0ab

Reported to the ECHA (European Chemicals Agency) database. (2012b). 2,6,10,15,19,23-hexamethyltetracosane: skin irritation/corrosion: 005 supporting | experimental result. https://echa.europa.eu/registration-dossier/-/registered-dossier/14412/7/4/2/?documentUUID=f5430888-c730-4e03-84b2-f5d276045549

Reported to the ECHA (European Chemicals Agency) database. (2012c). 2,6,10,15,19,23-hexamethyltetracosane: skin irritation/corrosion: 006 supporting | experimental result. https://echa.europa.eu/registration-dossier/-/registered-dossier/14412/7/4/2/?documentUUID=b6e76750-0873-416b-a0e5-f4d477e95137

Reported to the ECHA (European Chemicals Agency) database. (2012d). 2,6,10,15,19,23-hexamethyltetracosane: skin sensitisation: 004 supporting | experimental result. https://echa.europa.eu/registration-dossier/-/registered-dossier/14412/7/5/2/?documentUUID=c1f6e56c-b3f5-4fc4-8087-10cafd67741b

Reported to the ECHA (European Chemicals Agency) database. (2012e). 2,6,10,15,19,23-hexamethyltetracosane: biodegradation in water: screening tests: 004 supporting | experimental result. https://echa.europa.eu/registration-dossier/-/registered-dossier/14412/5/3/2/?documentUUID=1f1f792c-0997-4f6d-afc3-f90103cab0ab

Reported to the ECHA (European Chemicals Agency) database. (2013a). 2,6,10,15,19,23-hexamethyltetracosane: genetic toxicity: in vitro: 003 key | experimental result. https://echa.europa.eu/registration-dossier/-/registered-dossier/14412/7/7/2/?documentUUID=984c0b4e-2081-459e-9172-3780e9028006

Reported to the ECHA (European Chemicals Agency) database. (2013b). 2,6,10,15,19,23-hexamethyltetracosane: genetic toxicity: in vitro: 004. https://echa.europa.eu/registration-dossier/-/registered-dossier/14412/7/7/2/?documentUUID=737a6cc5-a15a-40fb-8db8-80272a7562ed

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Reported to the ECHA (European Chemicals Agency) database. (2013e). 2,6,10,15,19,23-hexamethyltetracosane: toxicity to reproduction. https://echa.europa.eu/registration-dossier/-/registered-dossier/14412/7/9/2

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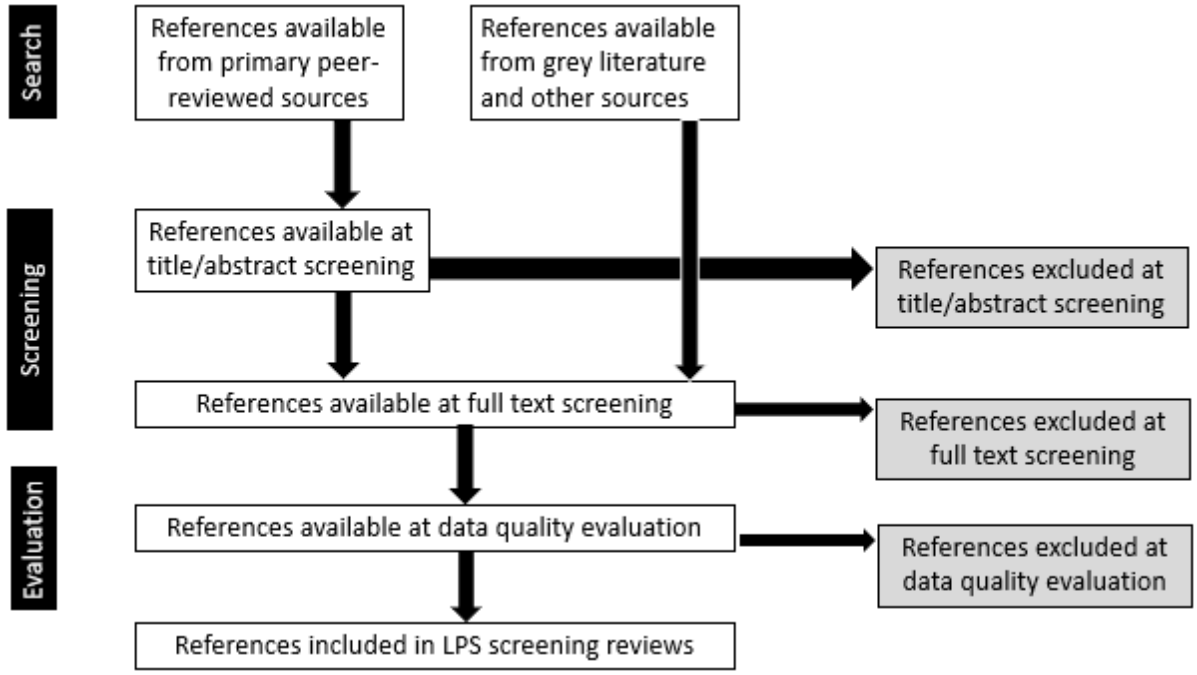
Appendix C: Literature Search Outcomes

C.1 Literature Search and Review

This section briefly describes the literature search and review process, search terms, and search outcomes for the hazard and fate screening of squalane. Search outcomes and reference details are provided on the candidate's HERO[47] project page.

EPA created a fit-for-purpose process to transparently document the literature search and review[48] of available hazard and fate information for low-priority substance (LPS) candidates. References from peer-reviewed primary sources, grey sources,[49] and other sources were identified, screened at the title/abstract and full-text level, and evaluated for data quality based on discipline-specific criteria. An overview of the literature search and review process is illustrated in Figure C1.

Figure C.1: Overview of the Literature Search and Review Process



[47] The HERO low-priority substance candidate project pages are accessible to the public at https://hero.epa.gov/hero/.

[48] Discussed in the document "Approach Document for Screening Hazard Information for Low-Priority Substances Under TSCA."

[49] Grey literature and additional sources are the broad category of studies not found in standard, peer-reviewed literature database searches. This includes U.S. and international government agency websites, non-government organization (NGO) websites, and data sources that are difficult to find, or are not included, in the peer-reviewed databases, such as white papers, conference proceedings, technical reports, reference books, dissertations, and information on various stakeholder websites.

C.1.1 Search Terms and Results

EPA began the literature review process for the hazard screening of squalane by developing search terms. To gather publicly available information, specific search terms were applied for each discipline and across databases and grey literature sources. Table C.1 lists the search terms used in the database search of peer -reviewed literature for squalane, while Table C.2 lists the search terms used for grey literature and other secondary sources.

Table C.1: Search Terms Used in Peer Reviewed Databases

Discipline	Database	Search terms[50]
Human Health	PubMed	111-01-3[rn] OR "2,6,10,15,19,23-Hexamethyltetracosane"[tw] OR "Hexamethyltetracosane"[tw] OR "Perhydrosqualene"[tw] OR "Squalan"[tw] OR "Squalane"[tw] OR "2,6,10,15,19,23-Hexamethyltetra-cosane"[tw] OR "2,6,10,15,19,23-Hexamethyltetracosan"[tw] OR "Dodecahydrosqualene"[tw] OR "Hexamethyl tetracosane"[tw] OR "Phytosqualan"[tw] OR "Phtyosqualan"[tw] OR "Tetracosane, 2,6,10,15,19,23-hexamethyl-"[tw] OR "Cetiol SQ"[tw] OR "Cosbiol"[tw] OR "Fitoderm"[tw] OR "Mild Finish 20P"[tw] OR "Phytiane LS"[tw] OR "Pripure 3759"[tw] OR "Pripure 379"[tw] OR "Pripure SQV 3759"[tw] OR "Robane"[tw] OR "Spinacane"[tw] OR "SQ-CONO"[tw] OR "Vitabiosol"[tw]
	Toxline	(111-01-3[rn] OR "2,6,10,15,19,23-Hexamethyltetracosane" OR "Hexamethyltetracosane" OR "Perhydrosqualene" OR "Squalan" OR "Squalane") AND (ANEUPL [org] OR BIOSIS [org] OR CIS [org] OR DART [org] OR EMIC [org] OR EPIDEM [org] OR FEDRIP [org] OR HEEP [org] OR HMTC [org] OR IPA [org] OR RISKLINE [org] OR MTGABS [org] OR NIOSH [org] OR NTIS [org] OR PESTAB [org] OR PPBIB [org]) AND NOT PubMed [org] AND NOT pubdart [org] "2,6,10,15,19,23-Hexamethyltetra-cosane" OR "2,6,10,15,19,23-Hexamethyltetracosan" OR "Dodecahydrosqualene" OR "Hexamethyl tetracosane" OR "Phytosqualan" OR "Phtyosqualan" OR "Tetracosane, 2,6,10,15,19,23-hexamethyl-" OR "Cetiol SQ" OR "Cosbiol" OR "Fitoderm" OR "Mild Finish 20P" OR "Phytiane LS" OR "Pripure 3759" OR "Pripure 379" OR "Pripure SQV 3759" OR "Robane" OR "Spinacane" OR "SQ-CONO" OR "Vitabiosol"
	TSCATS 1	111-01-3[rn] AND TSCATS[org]
	WOS	TS=("111-01-3" OR "2,6,10,15,19,23-Hexamethyltetracosane" OR "Hexamethyltetracosane" OR "Perhydrosqualene" OR "Squalan" OR "Squalane" OR "2,6,10,15,19,23-Hexamethyltetra-cosane" OR "2,6,10,15,19,23-Hexamethyltetracosan" OR "Dodecahydrosqualene" OR "Hexamethyl tetracosane" OR "Phytosqualan" OR "Phtyosqualan" OR "Tetracosane, 2,6,10,15,19,23-hexamethyl-" OR "Cetiol SQ" OR "Cosbiol" OR "Fitoderm" OR "Mild Finish 20P" OR "Phytiane LS" OR "Pripure 3759" OR "Pripure 379" OR "Pripure SQV 3759" OR "Robane" OR "Spinacane" OR "SQ-CONO" OR "Vitabiosol") AND ((WC=("Toxicology" OR "Endocrinology & Metabolism" OR "Gastroenterology & Hepatology" OR "Gastroenterology & Hepatology" OR "Hematology" OR "Neurosciences"

[50] Additional language or syntax such as [tw], [rn], [org], and [nm] were added to search terms. These are unique to individual databases and must be applied to search terms so that the query can run properly.

Table C.1: Search Terms Used in Peer Reviewed Databases		
		OR "Obstetrics & Gynecology" OR "Pharmacology & Pharmacy" OR "Physiology" OR "Respiratory System" OR "Urology & Nephrology" OR "Anatomy & Morphology" OR "Andrology" OR "Pathology" OR "Otorhinolaryngology" OR "Ophthalmology" OR "Pediatrics" OR "Oncology" OR "Reproductive Biology" OR "Developmental Biology" OR "Biology" OR "Dermatology" OR "Allergy" OR "Public, Environmental & Occupational Health") OR SU=("Anatomy & Morphology" OR "Cardiovascular System & Cardiology" OR "Developmental Biology" OR "Endocrinology & Metabolism" OR "Gastroenterology & Hepatology" OR "Hematology" OR "Immunology" OR "Neurosciences & Neurology" OR "Obstetrics & Gynecology" OR "Oncology" OR "Ophthalmology" OR "Pathology" OR "Pediatrics" OR "Pharmacology & Pharmacy" OR "Physiology" OR "Public, Environmental & Occupational Health" OR "Respiratory System" OR "Toxicology" OR "Urology & Nephrology" OR "Reproductive Biology" OR "Dermatology" OR "Allergy")) OR (WC="veterinary sciences" AND (TS="rat" OR TS="rats" OR TS="mouse" OR TS="murine" OR TS="mice" OR TS="guinea" OR TS="muridae" OR TS=rabbit* OR TS=lagomorph* OR TS=hamster* OR TS=ferret* OR TS=gerbil* OR TS=rodent* OR TS="dog" OR TS="dogs" OR TS=beagle* OR TS="canine" OR TS="cats" OR TS="feline" OR TS="pig" OR TS="pigs" OR TS="swine" OR TS="porcine" OR TS=monkey* OR TS=macaque* OR TS=baboon* OR TS=marmoset*)) OR (TS=toxic* AND (TS="rat" OR TS="rats" OR TS="mouse" OR TS="murine" OR TS="mice" OR TS="guinea" OR TS="muridae" OR TS=rabbit* OR TS=lagomorph* OR TS=hamster* OR TS=ferret* OR TS=gerbil* OR TS=rodent* OR TS="dog" OR TS="dogs" OR TS=beagle* OR TS="canine" OR TS="cats" OR TS="feline" OR TS="pig" OR TS="pigs" OR TS="swine" OR TS="porcine" OR TS=monkey* OR TS=macaque* OR TS=baboon* OR TS=marmoset* OR TS="child" OR TS="children" OR TS=adolescen* OR TS=infant* OR TS="WORKER" OR TS="WORKERS" OR TS="HUMAN" OR TS=patient* OR TS=mother OR TS=fetal OR TS=fetus OR TS=citizens OR TS=milk OR TS=formula OR TS=epidemio* OR TS=population* OR TS=exposure* OR TS=questionnaire OR SO=epidemio*)) OR TI=toxic* OR TS=metaboli* OR TS=biotransform* OR ((TS="breakdown" OR TS="break-down") AND (TS=product OR TS=products))) Indexes=SCI-EXPANDED, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, CCR-EXPANDED, IC Timespan=All years
Environmental Hazard	WOS	TS=("111-01-3" OR "2,6,10,15,19,23-Hexamethyltetracosane" OR "Hexamethyltetracosane" OR "Perhydrosqualene" OR "Squalan" OR "Squalane" OR "2,6,10,15,19,23-Hexamethyltetra-cosane" OR "2,6,10,15,19,23-Hexamethyltetracosan" OR "Dodecahydrosqualene" OR "Hexamethyl tetracosane" OR "Phytosqualan" OR "Phtyosqualan" OR "Tetracosane, 2,6,10,15,19,23-hexamethyl-" OR "Cetiol SQ" OR "Cosbiol" OR "Fitoderm" OR "Mild Finish 20P" OR "Phytiane LS" OR "Pripure 3759" OR "Pripure 379" OR "Pripure SQV 3759" OR "Robane" OR "Spinacane" OR "SQ-CONO" OR "Vitabiosol") AND ((WC=("Agriculture, Dairy & Animal Science" OR "Biodiversity Conservation" OR "Biology" OR "Developmental Biology" OR "Ecology" OR "Entomology" OR "Environmental Sciences" OR "Environmental Studies" OR "Fisheries" OR "Forestry" OR "Limnology" OR "Marine & Freshwater Biology" OR "Microbiology" OR "Mycology" OR

Table C.1: Search Terms Used in Peer Reviewed Databases		
		"Oceanography" OR "Ornithology" OR "Plant Sciences" OR “Reproductive Biology” OR "Zoology")) OR (SU=("Agriculture" OR "Biodiversity & Conservation" OR “Developmental Biology” OR "Entomology" OR "Environmental Sciences & Ecology" OR "Fisheries" OR "Forestry" OR "Marine & Freshwater Biology" OR "Microbiology" OR "Mycology" OR "Plant Sciences" OR “Reproductive Biology” OR "Zoology" OR "Oceanography")) OR (TI=toxic*) OR (TS=(ecotox* OR environment* OR phytotox* OR pollut* OR "A. platyrhynchos" OR "agnatha" OR "agnathan" OR "alligator" OR "alligators" OR "amphibian" OR "amphibians" OR "amphipod" OR "amphipoda" OR "amphipods" OR "Anas platyrhynchos" OR "annelid" OR "annelida" OR "annelids" OR "Antilocapridae" OR "apidae" OR "Aplodontidae" OR "Apoidea" OR "aquatic" OR "archiannelid" OR "archiannelida" OR "Arvicolinae" OR "aves" OR "avian" OR "avians" OR "badger" OR "badgers" OR "barnacle" OR "barnacles" OR "bass" OR "bear" OR "bears" OR "beaver" OR "beavers" OR "bee" OR "bees" OR "bird" OR "birds" OR "bivalve" OR "bivalves" OR "bleak" OR "bluegill" OR "bluegills" OR "bluehead" OR "bobwhite" OR "bobwhites" OR "Bovidae" OR "C. carpio" OR "caiman" OR "Canidae" OR "carp" OR "Castoridae" OR "catfish" OR "cephalopod" OR "cephalopoda" OR "cephalopods" OR "Cervidae" OR "chicken" OR "chickens" OR "chiselmouth" OR "clam" OR "clams" OR "cockle" OR "cockles" OR "cod" OR "copepod" OR "copepoda" OR "copepods" OR "coturnix" OR "crab" OR "crabs" OR "crappie" OR "crappies" OR "crayfish" OR "croaker" OR "crocodile" OR "crocodiles" OR "crustacea" OR "crustacean" OR "crustaceans" OR "Cyprinus carpio" OR "D. magna" OR "D. rerio" OR "dace" OR "Danio rerio" OR "daphnia" OR "Daphnia magna" OR "darter" OR "darters" OR "Dasypodidae" OR "Dicotylidae" OR "Didelphidae" OR "Dipodidae" OR "dog" OR "dogs" OR "dogfish" OR "duck" OR "duckling" OR "ducklings" OR "ducks" OR "earthworm" OR "earthworms" OR "ec50" OR "ec50s" OR "echinoderm" OR "echinoderms" OR "eel" OR "eels" OR "elasmobranch" OR "Equidae" OR "Erethizontidae" OR "Felidae" OR "ferret" OR "fish" OR "fisher" OR "fishers" OR "fishes" OR "flagfish" OR "flatworm" OR "flatworms" OR "flounder" OR "frog" OR "frogs" OR "galaxias" OR "gallus" OR "gastropod" OR "gastropoda" OR "gastropods" OR "Geomyidae" OR "goldfish" OR "gourami" OR "gouramy" OR "Green Algae" OR "grunion" OR "guppies" OR "guppy" OR "haddock" OR "hagfish" OR "haplodrili" OR "Harvest mice " OR "Harvest mouse" OR "herring" OR "Heteromyidae" OR "honeybee" OR "honeybees" OR "hooknose" OR "inanga" OR "killifish" OR "L. idus" OR "L. macrochirus" OR "lamprey" OR "lampreys" OR "lc50" OR "lc50s" OR "leech" OR "lemming" OR "Lepomis macrochirus" OR "Leporidae" OR "lethal concentration" OR "Leuciscus idus" OR "lizard" OR "lizards" OR "lobster" OR "lobsters" OR "macroinvertebrate" OR "macroinvertebrates" OR "mallard" OR "mallards" OR "marten" OR "medaka" OR "menhaden" OR "Microtus" OR "milkfish" OR "mink" OR "minnow" OR "minnows" OR "mollusc" OR "molluscs" OR "mollusk" OR "mollusks" OR "molly" OR "mrigal" OR "mudfish" OR "mudsucker" OR "mulles" OR "mullet" OR "mummichog" OR "mummichogs" OR "mussel" OR "mussels" OR "Mustelidae" OR "Myocastoridae" OR "Mysid shrimp" OR "newt" OR "newts" OR "northern pike" OR "O. latipes" OR "O. mykiss" OR "Ochotonidae" OR

Table C.1: Search Terms Used in Peer Reviewed Databases		
		"octopi" OR "octopus" OR "oligochaeta" OR "oligochaete" OR "Oncorhynchus mykiss" OR "Onychomys" OR "opossum" OR "Oryzias latipes" OR "oyster" OR "oysters" OR "P. promelas" OR "P. reticulata" OR "P. subcapitata" OR "perch" OR "Peromyscus" OR "Pimephales promelas" OR "pinfish" OR "pinfishes" OR "planaria" OR "planarian" OR "Poecilia reticulata" OR "polychaeta" OR "polychaete" OR "polychaetes" OR "Procyonidae" OR "Pseudokirchneriella subcapitata" OR "puffer" OR "puffers" OR "pumpkinseed" OR "pumpkinseeds" OR "pupfish" OR "quahog" OR "quahogs" OR "quail" OR "quails" OR "rasbora" OR "rasboras" OR "Reithrodontomys" OR "reptile" OR "reptiles" OR "rohu" OR "S. erythrophthalmus" OR "S. quadricauda" OR "S. subspicatus" OR "salamander" OR "salamanders" OR "salmon" OR "scallop" OR "scallops" OR "Scardinius erythrophthalmus" OR "Scenedesmus quadricauda " OR "Scenedesmus subspicatus" OR "Sciuridae" OR "sea anemone" OR "sea anemones" OR "sea cucumber" OR "sea cucumbers" OR "sea urchin" OR "sea urchins" OR "seabass" OR "seabream" OR "shark" OR "sharks" OR "shiner" OR "shiners" OR "shrimp" OR "Sigmodon" OR "Sigmodontinae" OR "silverside" OR "silversides" OR "skunk" OR "skunks" OR "snake" OR "snakehead" OR "snakes" OR "songbird" OR "songbirds" OR "Soricidae" OR "squid" OR "starfish" OR "stickleback" OR "sticklebacks" OR "sting ray" OR "sting rays" OR "sucker" OR "suckers" OR "Suidae" OR "sunfish" OR "Talpidae" OR "teleost" OR "teleostei" OR "teleosts" OR "terrapin" OR "terrapins" OR "tilapia" OR "tilapiaz" OR "toad" OR "toadfish" OR "toadfishes" OR "toads" OR "tortoise" OR "tortoises" OR "trout" OR "tubificid" OR "tubificidae" OR "tubificids" OR "turkey" OR "turkeys" OR "turtle" OR "turtles" OR "Ursidae" OR "vole" OR "walleye" OR "walleyes" OR "water flea" OR "water fleas" OR "waterbird" OR "waterbirds" OR "waterfowl" OR "waterfowls" OR "weakfish" OR "weasel" OR "whelk" OR "whelks" OR "wildlife"))) Indexes=SCI-EXPANDED, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, CCR-EXPANDED, IC Timespan=All years
	Toxline	Same as human health strategy synonyms only
	TSCATS 1	Same as human health strategy CASRN only
	Proquest	TITLE=("111-01-3" OR "2,6,10,15,19,23-Hexamethyltetracosane" OR "Hexamethyltetracosane" OR "Perhydrosqualene" OR "Squalan" OR "Squalane" OR "Dodecahydrosqualene" OR "Hexamethyl tetracosane" OR "Tetracosane, 2,6,10,15,19,23-hexamethyl-" OR "Mild Finish 20P") OR ABSTRACT=("111-01-3" OR "2,6,10,15,19,23-Hexamethyltetracosane" OR "Hexamethyltetracosane" OR "Perhydrosqualene" OR "Squalan" OR "Squalane" OR "Dodecahydrosqualene" OR "Hexamethyl tetracosane" OR "Tetracosane, 2,6,10,15,19,23-hexamethyl-" OR "Mild Finish 20P") OR SUBJECT=("111-01-3" OR "2,6,10,15,19,23-Hexamethyltetracosane" OR "Hexamethyltetracosane" OR "Perhydrosqualene" OR "Squalan" OR "Squalane" OR "Dodecahydrosqualene" OR "Hexamethyl tetracosane" OR "Tetracosane, 2,6,10,15,19,23-hexamethyl-" OR "Mild Finish 20P") "2,6,10,15,19,23-Hexamethyltetra-cosane" OR "2,6,10,15,19,23-Hexamethyltetracosan" OR "Phytosqualan" OR "Phtyosqualan" OR "Cetiol

Table C.1: Search Terms Used in Peer Reviewed Databases		
		SQ" OR "Cosbiol" OR "Fitoderm" OR "Phytiane LS" OR "Pripure 3759" OR "Pripure 379" OR "Pripure SQV 3759" OR "Robane" OR "Spinacane" OR "SQ-CONO" OR "Vitabiosol"
Fate	WOS	TS=("111-01-3" OR "2,6,10,15,19,23-Hexamethyltetracosane" OR "Hexamethyltetracosane" OR "Perhydrosqualene" OR "Squalan" OR "Squalane" OR "2,6,10,15,19,23-Hexamethyltetra-cosane" OR "2,6,10,15,19,23-Hexamethyltetracosan" OR "Dodecahydrosqualene" OR "Hexamethyl tetracosane" OR "Phytosqualan" OR "Phtyosqualan" OR "Tetracosane, 2,6,10,15,19,23-hexamethyl-" OR "Cetiol SQ" OR "Cosbiol" OR "Fitoderm" OR "Mild Finish 20P" OR "Phytiane LS" OR "Pripure 3759" OR "Pripure 379" OR "Pripure SQV 3759" OR "Robane" OR "Spinacane" OR "SQ-CONO" OR "Vitabiosol") AND TS=(adsorp* OR aerob* OR anaerob* OR bioaccumulat* OR bioavail* OR bioconcentrat* OR biodegrad* OR biomoni* OR biotrans* OR degrad* OR dispers* OR fish* OR hydroly* leach* OR migrat* OR partic* OR partition* OR persisten* OR photoly* OR volatil* OR abiotic OR absorb OR absorption OR accumulation-rate OR aerosol OR aerosols OR air OR anoxic OR atm-m3/mol OR biomagnification OR biosolids OR biota OR breakdown-product OR breakdown-products OR chelation OR coagulation complexation OR decay-rate OR diffusion-coefficient OR dissolution OR dust OR effluent OR environmental-fate OR evaporation-from-water OR excretion OR flocculation OR flux OR fugacity OR gas-phase-mass-transfer OR ground-water OR groundwater OR half-life OR henry's-law OR incinerate OR incineration OR indoor-outdoor-ratio OR influent OR ingestion OR intake OR kinetics OR liquid-phase-mass-transfer OR mass-transfer-coefficient OR microcosm OR modified-state-space OR particle-size OR particulate OR pathway OR pathways OR penetration-factor OR penetration-ratio OR photostability OR placenta OR plasma OR plume OR point-source OR point-sources OR pore-water OR pretreatment-program OR redox OR sediment OR serum OR sewage-treatment OR sludge OR soil OR subsurface-intrusion OR surface-water-concentration OR time-weighted-average OR transfer OR transformation OR trophic-magnification OR vapor OR wait-time OR wastewater-treatment OR weight-fraction OR wildlife OR BAF OR BCF OR BSAF OR BSAFs OR KAW OR Kd OR KOA OR KOC OR POTW OR SES OR WWTP OR ((OECD OR OPPTS OR OCSPP) AND (Guideline OR guidelines))) Indexes=SCI-EXPANDED, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, CCR-EXPANDED, IC Timespan=All years

Table C.2: Search Terms Used in Grey Literature and Additional Sources	
Chemical	**Search terms**
Squalane	Searched as a string or individually depending on resource: "111-01-3" OR "2,6,10,15,19,23-Hexamethyltetracosane" OR "Hexamethyltetracosane" OR "Perhydrosqualene" OR "Squalan" OR "Squalane" OR "2,6,10,15,19,23-Hexamethyltetra-cosane" OR "Dodecahydrosqualene" OR "Hexamethyl tetracosane" OR "Tetracosane, 2,6,10,15,19,23-hexamethyl-"

After the search terms were applied, more than 750 references were returned by all search efforts across peer-reviewed databases and grey literature sources. The total number of references include database

results and additional strategies. All references from the search efforts were screened and evaluated through the LPS literature search and review process.[48] Of these, 29 references were included for data evaluation and used to support the designation of squalane as LPS. The included hazard and fate references are listed in the bibliography of Appendix B.

C.2 Excluded Studies and Rationale

This section lists the excluded references, by HERO ID, found to be off-topic or unacceptable for use in the hazard screening of squalane. The excluded references are organized by discipline (human health hazard, environmental hazard, and fate), presented along with a rationale based on exclusion criteria. The criteria[48] was used to determine off-topic references in the title/abstract or full-text screening and to determine unacceptable references in the data quality evaluation are provided in the form of questions.

C.2.1 Human Health Hazard Excluded References

For the screening review of squalane, EPA excluded a total of 173 references when assessing human health hazard. Off-topic references (e.g., studies that did not contain information relevant to human health) were excluded at either title/abstract screening (see Table C.3), or full-text screening (see Table C.4). Unacceptable references (e.g., studies that did not meet data quality metrics) were excluded at full-text screening (see Table C.5). Off-topic and unacceptable references are displayed next to the corresponding exclusion criteria.

Table C.3: Off-Topic References Excluded at Title/Abstract Screening for Human Health Hazard									
Reference excluded (HERO ID) because the reference did NOT contain information needs[51] relevant to human health hazard									
4968686	4220587	4968694	4968817	4968965	4969085	4969209	4969269	4969193	4969258
900143	4220639	4968695	4968818	4968974	4969087	4969213	4969302	4969194	4969259
1085060	4220663	4968696	4968819	4968975	4969089	4969214	4969308	4969196	4969260
1169594	4271866	4968697	4968822	4968976	4969092	4969243	4969318	4969203	4969261
1525453	4293599	4968725	4968877	4968977	4969093	4969244	4969323	4969205	4969265
2337930	4332124	4968728	4968882	4968980	4969094	4969245	4969325	4969206	4969266
2463015	4354932	4968733	4968888	4968984	4969098	4969246	4969326	4969207	4969268
2464268	4654666	4968734	4968889	4969014	4969100	4969248	4969334	4968896	4968811
2551928	4864460	4968735	4968890	4969015	4969188	4969250	4969022	4968897	4968812
2568604	4886462	4968802	4968891	4969016	4969189	4969253	4969059	4968917	4968813
2576167	4947185	4968804	4968892	4969017	4969191	4969255	4969071	4968918	4968814
2582128	4968663	4968805	4968893	4969018	4968691	3603188	4969073	4968922	4968816
3005691	4968682	4968806	4968894	4969020	4968693	3813615	4969075	3014628	4968685
3005703	4968683	3014637							
Reference excluded (HERO ID) because the reference primarily contained *in silico* data									
N/A									

Table C.4: Screening Questions and Off-Topic References Excluded at Full-Text Screening for Human Health Hazard		
Question	**Off-topic if answer is:**	**References excluded (HERO ID)**
Does the reference contain information pertaining to a low- priority substance candidate?	No	76242 1618382 2052970

[51] The information needs for human health hazard includes a list of study characteristics pertaining to the study population/test organism, types of exposures and routes, use of controls, type and level of effects. A complete list of the information needs is provided in Table A1 of the "Approach Document for Screening Hazard Information for Low-Priority Substances Under TSCA". These information needs helped guide the development of questions for title/abstract and full-text screening.

Table C.4: Screening Questions and Off-Topic References Excluded at Full-Text Screening for Human Health Hazard		
Question	**Off-topic if answer is:**	**References excluded (HERO ID)**
		4968657 4968658 4968766 4968809 4968878 4969078
What type of source is this reference?	Review article or book chapter that contains only citations to primary literature sources	4968716
What kind of evidence does this reference primarily contain?	*In silico* studies that DO NOT contain experimental verification	N/A
The following question apply to HUMAN evidence only		
Does the reference report an exposure route that is or is presumed to be by an inhalation, oral, or dermal route?	No	N/A
Does the reference report both test substance exposure(s) AND related health outcome(s)?	No	N/A
If the reference reports an exposure to a chemical mixture, are measures of the test substance or related metabolite(s) reported independently of other chemicals? Note: If the paper does not pertain to mixtures, choose "Not Applicable".	No	N/A
The following question apply to ANIMAL evidence only		
Does the reference report an exposure route that is by inhalation, oral, or dermal route?	No	N/A
Does the reference report both test substance-related exposure(s) AND related health outcome(s)?	No	N/A
Does the reference report the duration of exposure?	No	4968724
Does the reference report an exposure to the test substance only (i.e. no mixtures with the exception	No	63197 4969080

Table C.4: Screening Questions and Off-Topic References Excluded at Full-Text Screening for Human Health Hazard		
Question	**Off-topic if answer is:**	**References excluded (HERO ID)**
of aqueous solutions and reasonable impurities and byproducts)?		1407194
Does the paper report a negative control that is a vehicle control or no treatment control?	No[52]	4968724
The following questions apply to MECHANISTIC/ALTERNATIVE TEST METHODS evidence only		
Does the reference report a negative control that is a vehicle control or no treatment control?	No	N/A
Does the reference report an exposure to the test substance only (i.e. no mixtures with the exception of aqueous solutions and reasonable impurities and byproducts)?	No	N/A
For genotoxicity studies only: Does the study use a positive control?	No	N/A

Table C.5: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Human Health Hazard – Animal		
Data Quality Metric	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 1: Test substance identity	• The test substance identity cannot be determined from the information provided (e.g., nomenclature was unclear and CASRN or structure were not reported). **OR** • For mixtures, the components and ratios were not characterized or did not include information that could result in a reasonable approximation of components.	N/A
Metric 2: Negative and vehicle controls	A concurrent negative control group was not included or reported. **OR** The reported negative control group was not appropriate (e.g., age/weight of animals differed between control and treated groups).	N/A

[52] Except for acute mammalian toxicity and skin and eye irritation studies, where the use of a negative control may not be required (e.g., OECD 403 Acute Inhalation Toxicity Guidelines).

Table C.5: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Human Health Hazard – Animal		
Data Quality Metric	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 3: Positive controls	When applicable, an appropriate concurrent positive control (i.e., inducing a positive response) was not used.	N/A
Metric 4: Reporting of doses/concentrations	Doses/concentrations were not reported and could not be calculated using default or reported estimates of body weight and diet/water intake (e.g., default intake values are not available for pregnant animals).	5016704 5016714 5016716 1619553 4968670 4968730 5016698 5016699 5016705 5016706
Metric 5: Exposure duration	The duration of exposure was not reported. **OR** The reported exposure duration was not suited to the study type and/or outcome(s) of interest (e.g., <28 days for repeat dose).	5016704 5016714 4968730 5016712
Metric 6: Test animal characteristics	The test animal species was not reported. **OR** The test animal (species, strain, sex, life-stage, source) was not appropriate for the evaluation of the specific outcome(s) of interest (e.g., genetically modified animals, strain was uniquely susceptible or resistant to one or more outcome of interest).	1619655 4829875 4968670 4968730
Metric 7: Number of animals per group	The number of animals per study group was not reported. **OR** The number of animals per study group was insufficient to characterize toxicological effects (e.g., 1-2 animals in each group).	N/A

Table C.5: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Human Health Hazard – Animal		
Data Quality Metric	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 8: Outcome assessment methodology	The outcome assessment methodology was not sensitive for the outcome(s) of interest (e.g., evaluation of endpoints outside the critical window of development, a systemic toxicity study that evaluated only grossly observable endpoints, such as clinical signs and mortality, etc.).	5016704 5016714 1619553 3044744 5016712
Metric 9: Reporting of data	Data presentation was inadequate (e.g., the report does not differentiate among findings in multiple exposure groups). **OR** Major inconsistencies were present in reporting of results.	5016714 4968730

C.2.2 Environmental Hazard

For the screening review of LPS candidate squalane, EPA excluded a total of 271 references when assessing environmental hazard. Off-topic environmental hazard references excluded at title/abstract screening are listed in Table C.6, and those excluded at full-text screening are listed in Table C.7. References in Table C.8 represent unacceptable studies based on specific data quality metrics for environmental hazard. Off-topic and unacceptable references are displayed next to the corresponding exclusion criteria.

Table C.6: Off-Topic References Excluded at Title/Abstract Screening for Environmental Hazard									
Reference excluded (HERO ID) because the reference did NOT contain information needs[53] relevant to environmental hazard									
4968714	4829875	4968715	4968823	4968863	4968905	2477014	4968992	4968768	1619655
4968898	4968645	4968716	4968824	4968865	4968906	2521944	4968997	4968769	1621432
4968899	4968646	4968717	4968825	4968866	4968907	2751432	4968999	4968770	1717019
4968901	4968647	4968719	4968826	4968868	4968908	2779061	4969000	4968772	1773844
4968903	4968648	4968720	4968828	4968871	4968909	2801478	4969001	4968773	1803070
4968910	4968649	4968721	4968829	4968872	4968911	2892109	4969003	4968775	1943411
4972318	4968650	4968722	4968830	4968873	4968915	2926805	4969008	4968776	2000216
63197	4968653	4968726	4968831	4968876	4968924	3009638	4969009	4968777	2035278
76242	4968654	4968730	4968832	4968878	4968925	3041256	4969011	4968778	2059619
658065	4968655	4968732	4968833	4968879	4968937	3041273	4969012	4968780	2130568

[53] The information needs for environmental hazard includes a list of study characteristics pertaining to the test organism/species, type and level of effects, and use of controls. A complete list of the information needs is provided in Table A2 of the "Approach Document for Screening Hazard Information for Low-Priority Substances Under TSCA". These information needs helped guide the development of questions for title/abstract and full-text screening.

Table C.6: Off-Topic References Excluded at Title/Abstract Screening for Environmental Hazard									
667025	4968656	4968737	4968834	4968880	4968950	3041274	4969013	4968781	2131264
790643	4968657	4968739	4968837	4968881	4968952	3041275	4969021	4968782	2134487
1011466	4968658	4968746	4968838	4968885	4968953	3041276	4969024	4968783	2151588
1328729	4968659	4968747	4968840	4968886	4968954	3041277	4969025	4968787	2157782
1407194	4968664	4968749	4968842	4968900	4968955	3041278	4969028	4968788	2167246
1485580	4968665	4968751	4968843	4968681	4968956	3044744	4969063	4968790	2173286
1485781	4968666	4968759	4968844	4968684	4968960	3075503	4969065	4968791	2174181
1487263	4968668	4968760	4968861	4968687	4968966	3471770	4969066	4968792	2185683
1560732	4968670	4968761	4968862	4968688	4968967	4066803	4969067	4968794	2196835
1618382	4968671	4968763	4969236	4968689	4968972	4168368	4969103	4968795	2202115
1619553	4968673	4968765	4969238	4968690	4968973	4441592	4969104	4968798	2214928
4968706	4968677	4968766	4971840	4968692	4968978	4602514	4969106	4968800	2242026
4968707	4968678	4968767	4972381	4968699	4968985	4663144	4969107	4968803	2303721
4968708	4968710	4812821	4972405	4968700	4968987	4671608	4969114	4968808	2310291
4968709	4968711	4969227	4997055	4968702	4968988	4687157	4969117	4969231	2369609
4968991	4968713	4774369	4999208	4968703	4968990	4733946	4969225	4999209	4968704
4968898	4968645	4968716	4968824	4968865	4968906	2521944	4968997	4968769	1621432
Reference excluded (HERO ID) because the reference did NOT present quantitative environmental hazard data									
N/A									

Table C.7: Screening Questions and Off-Topic References Excluded at Full-Text Screening for Environmental Hazard		
Question	**Off-topic if answer is:**	**References excluded (HERO ID)**
Does the reference contain information pertaining to a low-priority substance candidate?	No	4968663
What type of source is this reference?	Review article or book chapter that contains only citations to primary literature sources	N/A
Is quantitative environmental hazard data presented?	No	N/A
Is this primarily a modeling/simulation study? [Note: select "No" if experimental verification was included in the study]	Yes	N/A
Is environmental hazard data presented for standard or non-standard aquatic or terrestrial species (fish, invertebrates, microorganisms, non-mammalian terrestrial species)?	No	N/A
	Mixture	N/A

Table C.7: Screening Questions and Off-Topic References Excluded at Full-Text Screening for Environmental Hazard		
Question	**Off-topic if answer is:**	**References excluded (HERO ID)**
Is exposure measured for the target substance or is the test substance a mixture (except for reasonable impurities, byproducts, and aqueous solutions) or formulated product?	Formulated product	N/A
Does the reference report a duration of exposure?	No	N/A
Does the reference report a negative control that is a vehicle control or no treatment control?	No	N/A
Does the reference include endpoints in the information needs?	No	N/A

Table C.8: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Environmental Hazard		
Question	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 1: Test substance Identity	The test substance identity or description cannot be determined from the information provided (e.g., nomenclature was unclear, CASRN or structure were not reported, substance name/ description does not match CASRN). **OR** For mixtures, the components and ratios were not characterized or did not include information that could result in a reasonable approximation of components.	N/A
Metric 2: Negative controls	A concurrent negative control group was not included or reported.	N/A
Metric 3: Experimental system	The experimental system (e.g., static, semi-static, or flow-through regime) was not described.	N/A
Metric 4: Reporting of concentrations	Test concentrations were not reported.	N/A
Metric 5: Exposure duration	The duration of exposure was not reported. **OR** The reported exposure duration was not suited to the study type and/or outcome(s) of interest (e.g., study intended to assess effects on reproduction did not expose organisms for an acceptable period of time prior to mating).	N/A
Metric 6: Test Organism characteristics	The test species was not reported. **OR** The test species, life stage, or age was not appropriate for the outcome(s) of interest.	N/A

Table C.8: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Environmental Hazard		
Question	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 7: Outcome assessment methodology	The outcome assessment methodology was not reported.	N/A
Metric 8: Reporting of Data	Data presentation was inadequate. **OR** Major inconsistencies were present in reporting of results.	N/A

C.2.3 Fate

For the screening review of LPS candidate squalane, EPA excluded a total of 384 references when assessing environmental fate. Off-topic fate references excluded at title/abstract screening are listed in Table C.9, and those excluded at full-text screening are listed in Table C.10. References in Table C.11 represent unacceptable studies based on specific data quality metrics for fate. Off-topic and unacceptable references are displayed next to the corresponding exclusion criteria.

Table C.9: Off-Topic References Excluded at Initial Screening for Fate									
Reference excluded (HERO ID) because the reference did NOT contain information needs[54] relevant to environmental fate									
4972485	4969120	4380501	4972368	1053215	4969240	4868784	4972392	4968971	4972493
4968898	4969187	4421767	4972369	1165183	4969241	4879948	4972394	4968979	4972494
4968899	4969190	4439503	4972370	1165926	4969249	4885613	4972395	4968981	4972544
4968901	4969192	4653839	4972371	1176168	4969251	4890402	4972396	4968983	4972545
4968903	4969195	4707510	4972372	1179019	4969254	4968727	4972397	4969019	4972546
4968910	4969202	4711674	4972373	1179132	4969270	4968731	4972398	4969029	4972547
4972318	4969204	4712034	4972374	1180685	4969303	4968736	4972399	4969030	4972548
406362	4969208	4713766	4972375	1180952	4969306	4968738	4972400	4969031	4972549
610671	4969212	4718674	4972376	1207024	4969312	4968741	4972401	4969033	4972550
750416	4969215	4718675	4972379	1553568	4969320	4968742	4972402	4969034	4972551
750417	4969216	4718687	4972382	1559363	4972300	4968743	4972403	4969036	4972552
788234	4969217	4718688	4972383	1589053	4972301	4968744	4972404	4969037	4972553
862320	4969226	4731574	4972384	1643038	4972302	4968745	4972406	4969038	4972604
900107	4969228	4732081	4972385	1956791	4972303	4968748	4972407	4969039	4972605
912592	4969229	4865149	4972386	1958333	4972304	4968750	4972408	4969041	4972606

[54] The information needs for fate includes a list of study characteristics pertaining to the associated media and exposure pathways, associated processes, and use of controls. A complete list of the information needs is provided in Table A3 of the "Approach Document for Screening Hazard Information for Low-Priority Substances Under TSCA". These information needs helped guide the development of questions for title/abstract and full-text screening.

Table C.9: Off-Topic References Excluded at Initial Screening for Fate									
921506	4969232	4865185	4972387	1964775	4972305	4968752	4972434	4969044	4972607
958237	4969235	4865455	4972389	1964964	4972306	4968753	4972435	4969045	4972608
966159	4969237	4866874	4972390	2286747	4972307	4968754	4972436	4969046	4972609
972251	4969239	4868755	4972391	2339827	4972308	4968755	4972437	4969047	4972610
4972647	4972745	4969086	3012659	2541032	4972309	4968756	4972439	4969049	4972611
4972648	4972746	4969088	3035464	2825185	4972310	4968757	4972440	4969050	4972612
4972649	4999220	4969091	3038753	2831987	4972311	4968809	4972442	4969051	4972613
4972650	4999222	4969101	3044681	2911319	4972313	4968887	4972443	4969053	4972614
4972652	4999223	4969102	3220416	2912000	4972314	4968895	4972444	4969054	4972615
4972653	4999224	4969108	3312184	3005771	4972316	4968920	4972446	4969055	4972616
4972655	4999225	4969109	3340942	4972711	4972321	4968928	4972447	4969056	4972617
4972708	4999226	4969110	3457241	4972712	4972322	4968930	4972448	4969072	4972618
4972709	4999227	4969113	3457694	4972713	4972324	4968932	4972450	4969076	4972619
4972710	4999230	4969115	3459918	4972739	4972325	4968934	4972453	4969079	4972646
4972333	4968941	4969116	3579588	4972740	4972326	4968935	4972454	4969081	4972486
4972361	4968943	4969118	3868028	4972741	4972327	4968936	4972455	4969084	4972487
4972362	4968944	4969119	4186269	4972742	4972329	4968938	4972457	4968970	4972488
4972363	4968946	4972491	4351829	4972743	4972330	4968939	4972459	4972367	4972489
4972364	4968948	4972490	4377995	4972744	4972331	4968940			
Reference excluded (HERO ID) because the reference did NOT present quantitative environmental fate data									
N/A									

Table C.10: Screening Questions and Off-Topic References Excluded at Full-Text Screening for Fate		
Question	**Off-topic if answer is:**	**References excluded (HERO ID)**
Does the reference contain information pertaining to a low- priority substance candidate?	No	900143 1560732 2477014 4066803 4968706 4968730 4968761 4968775 4968776 4968825

Table C.10: Screening Questions and Off-Topic References Excluded at Full-Text Screening for Fate		
Question	**Off-topic if answer is:**	**References excluded (HERO ID)**
		4968826 4968833 4968838 4968840 4969008 4969073 4969214 4972393 4972438 4972441 4972451 4972654 4999221 4999229 4968702
What type of source is this reference?	Review article or book chapter that contains only citations to primary literature sources	N/A
Is quantitative fate data presented?	No	5016718
Is this primarily a modeling/simulation study? [Note: Select "Yes" only if there is no experimental verification]	Yes	2551928 2568604 3014628 3014637 3603188

Table C.11: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Fate		
Data quality metric	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 1: Test substance identity	The test substance identity or description cannot be determined from the information provided (e.g., nomenclature was unclear and CASRN or structure were not reported). **OR** For mixtures, the components and ratios were not characterized or did not include information that could result in a reasonable approximation of components.	N/A
Metric 2: Study controls	The study did not include or report crucial control groups that consequently made the study unusable (e.g., no positive control for a biodegradation study reporting 0% removal).	4968666 4968783 5016697

Table C.11: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Fate		
Data quality metric	**Unacceptable if:**	**References excluded (HERO ID)**
	OR The vehicle used in the study was likely to unduly influence the study results.	5016726 5016727
Metric 3: Test substance stability	There were problems with test substance stability, homogeneity, or preparation that had an impact on concentration or dose estimates and interfered with interpretation of study results.	N/A
Metric 4: Test method suitability	The test method was not reported or not suitable for the test substance. **OR** The test concentrations were not reported. **OR** The reported test concentrations were not measured, and the nominal concentrations reported greatly exceeded the substances water solubility, which would greatly inhibit meaningful interpretation of the outcomes.	N/A
Metric 5: Testing conditions	Testing conditions were not reported, and the omission would likely have a substantial impact on study results. **OR** Testing conditions were not appropriate for the method (e.g., a biodegradation study at temperatures that inhibit the microorganisms).	4968783 5016697
Metric 6: System type and design- partitioning	Equilibrium was not established or reported, preventing meaningful interpretation of study results. **OR** The system type and design (e.g. static, semi-static, and flow-through; sealed, open) were not capable of appropriately maintaining substance concentrations, preventing meaningful interpretation of study results.	N/A
Metric 7: Test organism-degradation	The test organism, species, or inoculum source were not reported, preventing meaningful interpretation of the study results.	N/A
Metric 8: Test organism-partitioning	The test organism information was not reported. **OR** The test organism is not routinely used and would likely prevent meaningful interpretation of the study results.	N/A
Metric 9: Outcome assessment methodology	The assessment methodology did not address or report the outcome(s) of interest.	4663144

Table C.11: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Fate		
Data quality metric	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 10: Data reporting	Insufficient data were reported to evaluate the outcome of interest or to reasonably infer an outcome of interest. **OR** The analytical method used was not suitable for detection or quantification of the test substance. **OR** Data indicate that disappearance or transformation of the parent compound was likely due to some other process.	4663144 5016697
Metric 11: Confounding variables	There were sources of variability and uncertainty in the measurements and statistical techniques or between study groups.	N/A
Metric 12: Verification or plausibility of results	Reported value was completely inconsistent with reference substance data, related physical-chemical properties, or otherwise implausible, indicating that a serious study deficiency exists (identified or not).	4663144