Supporting Information for Low-Priority Substance 1,2-Hexanediol (CASRN 6920-22-5)

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. 1,2-Hexanediol 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 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.

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

[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).

6(b)(1)(A) and 40 CFR 702.9. This paper documents the results of the screening review which supports the final designation of 1,2-hexandiol 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.

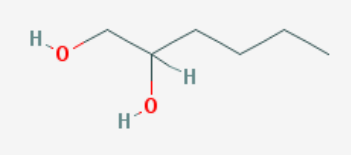
- *Appendix A (Conditions of Use Characterization):* This appendix contains a comprehensive list of TSCA and non-TSCA uses for the chemical substance from publicly available databases.

- *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 1,2-Hexanediol

Table 1 below provides the CAS number, synonyms, and other information on 1,2-hexanediol.

Table 1: 1,2-Hexanediol at a Glance	
Chemical Name	1,2-Hexanediol
CASRN	6920-22-5
Synonyms	Hexane-1,2-diol; 1,2-Dihydroxyhexane; 5,6-Dihydroxyhexane; DL-hexane-1,2-diol
Trade Name(s)	None found
Molecular Formula	$C_6H_{14}O_2$
Representative Structure	

1,2-Hexanediol is an alcohol in the diol (or glycol) family. It is an organic chemical compound containing two hydroxyl (-OH) groups on a six-carbon backbone. Because of the adjacent positioning of the two hydroxyl groups, 1,2-alkanediols contain a stereocenter, leading to two stereoisomers: *cis*-1,2-hexanediol and *trans*-1,2-hexanediol. Because the hydroxyl groups are located on the first and second carbons on one end of a six-carbon chain, 1,2-hexanediol is an amphiphilic molecule that acts as both a cosurfactant and solvent. A cosurfactant increases the effectiveness of surfactants, which are compounds containing both hydrophilic and hydrophobic moieties that work to lower the surface tension at an interface (e.g., between two liquids). Surfactants may function as detergents, emulsifiers, foaming agents, wetting agents, and dispersants in a variety of applications and product sectors. See Section 5 for 1,2-hexanediol's conditions of use.

In addition, 1,2-hexanediol is hygroscopic and thus acts as a humectant, which means that it absorbs water and increases hydration in products. Also, straight-chain 1,2-alkanediols, including 1,2-hexanediol, have broad spectrum antimicrobial properties and are used alone or in combination with other chemicals, to serve as preservatives and/or preservative boosters. These properties contribute to the use of 1,2-hexanediol as a multifunctional ingredient in products. Section 5 includes conditions of use for this chemical.

3. Physical-Chemical Properties

Table 2 lists the physical-chemical properties for 1,2-hexanediol. 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 1,2-hexanediol

Source/Model	Data Type	Endpoint	Endpoint value	Notes
Reported to the ECHA database, 2017	Experimental	State at room temperature	Liquid	Substance is a clear, colorless liquid at room temperature
Reported to the ECHA database, 2017	Calculated	Molecular weight	118 g/mol	Calculated from molecular formula C6 H14 O2
Lyman et al. 1990	Estimated	Molar volume	155 cm^3/mol	LeBas Molar Volume, calculated according to the volume parameters reported in Lyman et al., 1990
Johnson 2012	Experimental	Melting point	<25°C	Substance is a liquid at room temperature
Reported to the ECHA database, 2017	Experimental	Melting point	2°C	Reported as solidification temperature at 1 atm. ISO 1392. • Solidification temperature measured as the maximum temperature resulting from the solidification process as the chemical is cooled. • It was noted that the temperature rose during cooling as a result of heat of crystallization.
Reported to the ECHA database, 2017	Experimental	Boiling point	228.3 °C	Reported at standard atmospheric pressure. EU Method A.2 Siwoloboff method using photo cell detection.
EPISuite v4.11[4]	Estimated	Boiling point	220°C	
Reported to the ECHA database, 2017	Experimental	Vapor pressure	0.00432 mm Hg at 25°C (Reported as 0.576 Pa)	Estimated as $9.4x10^{-3}$ mm Hg
Johnson 2012	Experimental	Vapor pressure	0.0194 mm Hg	Unpublished data for commercial product Hydrolite-6 (99% 1,2-hexanediol).
EPISuite v4.11	Estimated	Vapor pressure	0.008 mm Hg	
Reported to the ECHA database, 2017	Experimental	Water solubility	9000 mg/L at 23.5°C	Reported as >9 g/g water at 23.5°C and pH 6.91. • Concluded to be miscible. EU Method A.6, flask method. • GLP compliant.
EPISuite v4.11	Estimated	Water solubility	$6.89x10^4$ mg/L	Experimental input values: MP = 2°C; log Kow = 0.58

[4] Physical properties used for estimation: Water Solubility 26171 mg/L, log Kow 0.69, SMILES: OCC(O)CCCC

Table 2: Physical-Chemical Properties for 1,2-hexanediol				
Source/Model	**Data Type**	**Endpoint**	**Endpoint value**	**Notes**
Reported to the ECHA database, 2017	Experimental	Log K_{ow}	0.58	Reported at 25°C and pH 7.09-7.49. • EU Method A.8; shake-flask method. • GLP compliant
Johnson 2012	Experimental	Log K_{ow}	0.25	Unpublished data for commercial product Hydrolite-6 (99% 1,2-hexanediol).
EPISuite v4.11	Estimated	Log K_{ow}	0.69	
EPISuitev4.11	Estimated	Henry's Law Constant	$7.5x10^{-8}$ atm-m^3/mole	Experimental input values: VP = $4.32x10^{-3}$ mm Hg; WS = $9x10^3$ mg/L
EPISuitev4.11	Estimated	Sediment/soil adsorption/ desorption - K_{oc}	2.6	Estimated as Log K_{oc} = 0.42.
EPISuitev4.11	Estimated	Level III fugacity model	Air: 1.3% Water: 38.2% Soil: 60.5% Sediment: 0.1%	Assumes equal emissions of 1,000 kg/hour to air, water, and soil (EPISuite default values)
EPISuitev4.11	Estimated	Atmospheric half-life	6.9 hours	Atmospheric half-life is estimated from a gas-phase rate constant, however, if any amount of this substance partitions to the atmosphere it is expected to exist as a solid
		Explosivity	No data located	
		Pyrolysis	No data located	
		pH	No data located	
Johnson 2012	Experimental	pKa	14.22	Unpublished data for commercial product Hydrolite-6 (99% 1,2-hexanediol)
EPISuitev4.11	Estimated	Wastewater treatment plant removal	94% Total Removal (93% biodegradation, 0.28% sludge, 0% air)	Input parameters: BIOP = 4, BioA = 1 and BioS = 1 based on 82.9% (average) removal after 28 days in non-adapted activated sludge, 10-day window met, Readily biodegradable OECD TG 301B: CO2 Evolution Test
EPISuitev4.11	Estimated	BCF	3.2	
EPISuitev4.11	Estimated	BAF	1.1	

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 form and measured melting point, 1,2-hexanediol is a liquid under ambient conditions. Because of its measured vapor pressure, 1,2-hexanediol is also expected to be volatile when present as a "neat" or undiluted substance (Reported to the ECHA database, 2017; Johnson, 2012). As a result, exposure to 1,2-hexanediol is possible through direct dermal contact with the substance and through inhalation of vapors or aerosols if they are generated. Based on measured data, 1,2-hexanediol is water soluble, indicating the potential for this substance to dissolve in water and form an aqueous solution (Reported to the ECHA database, 2017). Water soluble substances have an increased potential for absorption through the lungs; therefore, if inhalation of vapors or aerosols occurs, absorption through the lungs is likely. Exposure potential changes when 1,2-hexanediol is present in diluted form. The estimated Henry's Law constant for 1,2-hexanediol indicates volatilization from water and aqueous solutions (i.e., 1,2-hexanediol when diluted in water) will be minimal (US EPA, 2019) and therefore exposure through breathing vapor is expected to be minimal. The fact that 1,2-hexanediol is water soluble increases the potential for oral exposure via ingestion of contaminated drinking water, including well water. Oral exposure to this chemical could result in moderate absorption through the gastrointestinal tract. However, based on its estimated log K_{ow}, 1,2-hexanediol is unlikely to cross lipid membranes and sequester in fatty tissues, as confirmed by its estimated bioconcentration factor (BCF) and bioaccumulation factor (BAF) (US EPA, 2019). The estimated log K_{oc} indicates this substance is unlikely to adsorb to soil or sediment particles (US EPA, 2019). Based on the log K_{oc} and water solubility, 1,2-hexanediol is expected to be highly mobile in soils increasing its potential for leaching into, and transport in, groundwater, including well water. 1,2-Hexanediol is expected to have very low persistence (US EPA, 2019). Experimental data demonstrate it is readily biodegradable in aerobic conditions (discussed further in Section 6.3.1), and analog data indicate it is ultimately degradable anaerobically (discussed further in Section 6.3.1), meaning that if it were to enter groundwater, it is likely to be broken down into carbon dioxide and water.

3.1 References

Johnson, W., Bergfeld, W. F., Belsito, D. V., Hill, R. A., Klaassen, C. D., Liebler, D., Marks, J. G., Shank, R. C., Slaga, T. J., Snyder, P. W., Andersen, F. A. (2012). Safety Assessment of 1,2-Glycols as Used in Cosmetics. *International Journal of Toxicology, 31*, 147S-168S

European Chemicals Agency (ECHA). (2017). DL-hexane-1,2-diol. Retrieved from https://echa.europa.eu/registration-dossier/-/registered-dossier/11614

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

US 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 1,2-hexanediol and added the chemical to the Safer Choice Program's Safer Chemical Ingredients List (SCIL) in January 2016 under the functional class of solvents. The SCIL[6] is a continuously updated list of chemicals that meet low-concern Safer Choice criteria.[7]

Internationally, the German Environment Agency (UBA) designated 1,2-hexanediol as "low hazard to waters" (rating of 1) in March 2019 based on an assessment of ecotoxicity and environmental fate.[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://webrigoletto.uba.de/rigoletto/public/searchDetail.do?kennummer=4987

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 1,2-hexanediol (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 2016 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 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, 1,2-hexanediol is manufactured domestically and imported. It is a solvent used in processing (incorporation into article, and incorporation into formulation, mixture, or product) in the industrial printing ink manufacturing sector; as well as in ink, toner, and colorant products for consumer and commercial use (EPA 2017b). Based on the known manufacturing, processing, and uses of this chemical substance, EPA assumes distribution in commerce. Based on CDR, two facilities reported that 1,2-hexanediol was not recycled (e.g., not recycled, remanufactured, reprocessed, or reused). Another facility reported this information as confidential business information (CBI). No information on disposal is found in CDR or through EPA's Toxics Release Inventory (TRI) Program[10] because 1,2-hexanediol 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 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 uses or identify additional occupational[11] and consumer uses. This research improved the Agency's understanding of the conditions of use for 1,2-hexanediol. Although EPA identified uses of 1,2-hexanediol 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 1,2-hexanediol 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 1,2-Hexanediol			
Life Cycle Stage	**Category**	**Subcategory of Use**	**Source**
Manufacturing	Domestic manufacture	Domestic manufacture	EPA (2017b)
	Import	Import	
Processing	Processing- incorporation into article	Other use in printing ink manufacturing	EPA (2017b)
	Processing- incorporation into formulation, mixture or product	Solvents (which become part of product formulation or mixture) in printing ink manufacturing	
	Recycling	Recycling	EPA (2017b)[12]
Distribution	Distribution	Distribution	EPA (2017b)
Commercial uses	Ink, toner, and colorant products		EPA (2017b)
Consumer uses	Ink, toner, and colorant products	Printing ink	EPA (2017b)
Industrial/commercial/consumer uses	Fuel and lubricant additive	Fuel and lubricant additives	Ullmann's (2012)
Disposal	Releases and waste disposal	Releases to air, wastewater, solid and liquid wastes	Though not explicitly identified, releases from disposal were assumed to be reasonably foreseen[13]

[12] In the 2016 CDR, two facilities reported that 1,2-hexanediol was not recycled (e.g., not recycled, remanufactured, reprocessed, or reused). One facility reported this information as CBI (EPA 2017b).

[13] 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[14] 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 1,2-hexanediol against the endpoints listed below. EPA's New Chemicals Program has used these endpoints for decades to evaluate chemical substances under TSCA[15] 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[16] 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[17]	**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

[14] 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.

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

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

[17] 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)[18]		**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[19]		**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[20]	**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		

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

[19] 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).

[20] 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[21]	**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[22] evidence in humans)	Negative studies or robust mechanism-based SAR
Sensitization[23]		**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[24]	**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

[21] 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).

[22] 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".

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

[24] 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)[25]	**Chronic Aquatic Toxicity Value (L/E/IC50)[25]**	**Persistence (Measured in terms of level of biodegradation)[26]**	**Bioaccumulation Potential[27]**
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

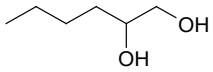
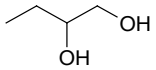
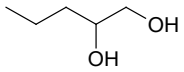
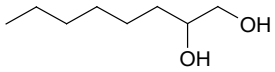
Below is a summary of the information that EPA included in the hazard evaluation of 1,2-hexanediol. In many cases, EPA used analogous chemicals to make findings for a given endpoint. Where this is the case, use of the analog is explained. If the chemical studied is not named, the study is for 1,2-hexanediol. Appendix B contains more information on each study used to assess hazards.

1,2-Hexanediol is a linear aliphatic diol with a carbon chain length containing six carbons. EPA used best professional judgement to select analogs for 1,2-hexanediol based on similarity in structure, molecular weight, and functionality, with the assumption that these chemicals will have similar physical-chemical properties, environmental transport and persistence characteristics, bioavailability, and toxicity profiles. As shown in Table 5, all analogs are linear aliphatic 1,2-diols like the candidate chemical, 1,2-hexanediol, and differ only in their chain lengths. 1,2-butanediol contains four carbons, pentylene glycol contains five carbons and 1,2-octanediol contains eight carbons.

[25] 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).*

[26] 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)*.

[27] 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.]

Table 5: 1,2-Hexanediol and Analogs Structures		
CASRN	Name	Structure
6920-22-5	1,2-Hexanediol	
584-03-2	1,2-Butanediol	
5343-92-0	Pentylene glycol	
1117-86-8	1,2-Octanediol	

6.1.1 Absorption, Distribution, Metabolism, Excretion

To review absorption, distribution, metabolism and excretion (ADME) endpoints without adequate quality[22] 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

If 1,2-hexanediol is inhaled as a vapor, dust, or aerosol, absorption through the lungs is likely based on its water solubility (discussed in Section 3).

The potential for dermal absorption of 1,2-hexanediol is predicted to be moderate based on its molecular weight, water solubility, and log K_{ow} (discussed in Section 3).

Further, in the event of oral ingestion, absorption across the GI tract is also predicted to be moderate based on its molecular weight, water solubility and log K_{ow} (discussed in Section 3).

Distribution

Following absorption through the lungs, skin, or GI tract, hexanediol is expected to be distributed via blood. Based on the log k_{ow} and water solubility (Section 3), 1,2-hexanediol is unlikely to cross lipid membranes or be sequestered in fatty tissues.

Metabolism

Experimental data determined to be of adequate quality[28] on 1,2-hexanediol metabolite formation were not reasonably available. The Quantitative Structure-Activity Relationship (QSAR) toolbox[29] was used to run the rat liver S9 metabolism simulator, the skin metabolism simulator, and the *in vivo* rat metabolism simulator. 1,2-Hexanediol is predicted to be absorbed and metabolized through oxidation and glucuronide conjugation metabolic pathways.[30] The QSAR toolbox was used to identify putative 1,2-hexanediol metabolites. *In vivo* metabolites are 2-hydroxyhexanoic acid and 2-hydroxyhexanal as potential metabolites.

Excretion

Following metabolism, 1,2-hexanediol and metabolites are expected to be excreted via urine due to the low molecular weight and water solubility (Section 3). No accumulation in the body is expected as a result of excretion through efficient metabolic pathways and the formation of soluble degradation products.

6.1.2 Acute Toxicity

EPA assessed the potential for mammalian toxicity from acute exposures to 1,2-hexanediol using the results of an OECD Guideline 401 study on rats exposed to the chemical by oral gavage. This study indicated low concern for acute exposures with an LD_{50} greater than the low-concern benchmark of 2000 mg/kg for both males and females (Reported to the ECHA database, 1981a).

EPA also assessed the potential for toxicity from acute dermal and inhalation exposures using read-across predictions from pentylene glycol. No adverse effects were observed in rats after a 24-hour dermal exposure to a 2000 mg/kg dose (Reported to the ECHA database, 1982a), indicating low concern for acute dermal exposure by having an LD_{50} greater than the 2000 mg/kg dermal low-concern benchmark. Further, no mortality was observed in rats after a 4-hour aerosol inhalation exposure to pentylene glycol, indicating low concern for acute exposures (Reported to the ECHA database, 1982b). The LD_{50} was greater than the low-concern benchmark of 5 mg/L.

These results provide sufficient information to indicate low concern for acute exposures to 1,2-hexanediol from oral, inhalation, and dermal exposure pathways.

6.1.3 Repeated Dose Toxicity

EPA assessed the potential for repeated dose mammalian toxicity based on the results of an OECD Guideline 411 90-day dermal, repeated dose study on rats exposed to 1,2-hexanediol. This study identified a repeated dose no observed adverse effect level (NOAEL) of 700 mg/kg-day, with a lowest observed adverse effect level (LOAEL) of 1000 mg/kg-day based on reduced body weight gain in males and females and increased total leukocyte count and urinary protein in females (Reported to the ECHA database, 2002a). These results provide sufficient information to indicate low

[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

[30] Final Report of the Cosmetic Ingredient Review Expert Panel: On the Safety Assessment of 1,2-Glycols as Used in Cosmetics. June 28, 2011.

concern for repeated dermal exposures to 1,2-hexanediol by exceeding the low-concern benchmark of 200 mg/kg-day for a 90-day exposure.

Oral repeated dose studies were available for the analogs pentylene glycol and 1,2-octanediol. In a 90-day oral gavage study in rats exposed to pentylene glycol, adverse effects were not observed in groups dosed up to the highest dose tested at 1000 mg/kg-day (Reported to the ECHA database, 2013). A 28-day study in rats exposed to 1,2 octanediol via oral gavage reported a NOAEL of 300 mg/kg-day and LOAEL of 1000 mg/kg-day based on slightly reduced locomotor activity and changes in organ weights (Reported to the ECHA database, 2004). These results from closely-related analogs provide sufficient information to indicate low concern for repeated oral exposures to 1,2-hexanediol by exceeding the low-concern benchmark of 100 mg/kg-day for a 90-exposure (300 mg/kg-day for a ~30-day exposure).

6.1.4 Reproductive and Developmental Toxicity

EPA assessed the potential for 1,2-hexanediol to cause mammalian reproductive toxicity using the OECD Guideline 411 90-day dermal, repeated dose study on rats discussed in Section 6.1.3. This study also examined estrous cycle evaluations in females and sperm parameters (sperm count, motility and morphology) in males. No adverse effects were noted for the evaluated reproductive parameters, resulting in a NOAEL of 1000 mg/kg-day (Reported to the ECHA database, 2002a, b). These results provide sufficient information to indicate low concern for reproductive and developmental toxicity based on the NOAEL exceeding the 500 mg/kg-bw/day low concern dermal benchmark.

To further assess the reproductive and developmental toxicity potential for 1,2-hexanediol, EPA evaluated two oral gavage studies in pregnant female rats exposed to 1,2-hexanediol. In the first study, results from exposure during gestation days 5-19 indicated no adverse maternal or developmental effects at the highest dose tested, resulting in a NOAEL of 300 mg/kg-day (Johnson et al., 2012; Reported to the ECHA database, 2006). In the second study, rats exposed during gestation days 6-19 to 1,2-hexanediol reported no developmental effects, resulting in a developmental NOAEL at the highest dose of the study, 750 mg/kg-day. However, the females exposed to 750 mg/kg-day displayed decreased absolute and relative feed consumption, leading to decreased body weight. The maternal NOAEL for this study was 500 mg/kg-day and the LOAEL was 750 mg/kg-day (Reported to the ECHA database, 2003a). These results taken with the low-concern oral benchmark of 250 mg/kg-day provide sufficient information to indicate low concern for reproductive and developmental toxicity.

6.1.5 Genotoxicity

EPA assessed experimental studies on chromosomal aberration and gene mutation as potential indicators of genotoxic carcinogenicity. Three *in vitro* gene mutation results on two different bacteria species and a cell line indicate negative results for gene mutation with and without metabolic activation (Reported to the ECHA database, 2013, 1998b). Chinese hamster ovarian cells exposed to 1,2-hexanediol were negative for chromosomal aberrations with and without metabolic activation (Reported to the ECHA database, 2000). These negative results provide sufficient information to indicate low concern for genotoxicity.

6.1.6 Carcinogenicity

Experimental data determined to be of adequate quality[31] on 1,2-hexanediol or closely-related analogs 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 1,2-hexanediol, 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.[32] For this chemical, there is an absence of the types of reactive structural features that are present in genotoxic carcinogens. ISS profiler, a QSAR model,[33] identified aldehyde as a potential metabolite alert; however, this metabolite is transient and expected to be further metabolized (see Figure 6 in the Metabolic Pathway Trees Supplemental Document[34]) Also, 1,2-hexanediol goes through multiple other detoxification pathways, including sulfation and glucuronidation transformations that do not lead to an aldehyde metabolite (see Figure 6 in the Metabolic Pathway Trees Supplemental Document).

The Virtual models for property Evaluation of chemicals within a Global Architecture (VEGA) models'[35] results indicate 1,2-hexanediol has low potential to be carcinogenic or mutagenic with moderate reliability.

Applying expert scientific judgement based on the reasonably available information and weight of scientific evidence, EPA finds that 1,2-hexanediol's transformation profile, a lack of structural alerts in the parent chemical substance, and experimental genotoxicity results provide sufficient information to indicate this chemical is unlikely to be carcinogenic or mutagenic.

6.1.7 Neurotoxicity

While no traditional neurotoxicity studies were reasonably available for 1,2-hexanediol or the closely-related analogs, EPA assessed the potential for neurotoxicity using relevant endpoints measured in a repeated dose study. The repeated dose oral studies in rats for the analogs pentylene glycol and 1,2-octanediol reported minimal or no effects on the limited neurological endpoints that were evaluated. No effects on functional observational battery (FOB) parameters and motor activity measurements at doses of pentylene glycol up to 1000 mg/kg-day in a 90-day study (highest dose tested) (Reported to

[31] 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

[32] "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.

[33] 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.

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

[35] 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.

the ECHA database, 2013). Slightly reduced locomotor activity was observed at 1000 mg/kg-day (LOAEL) in a 28-day oral study of 1,2-octanediol; however, no effects were observed on histopathology of the brain, spinal cord or sciatic nerve in this study (Reported to the ECHA database, 2004). These data from closely-related analogs provide sufficient information to indicate there is low concern for neurotoxicity associated with 1,2-hexanediol. This finding is also supported by the low-hazard findings for other human health hazard endpoints, including toxicity from acute and chronic exposures, reproductive toxicity, and developmental toxicity.

6.1.8 Skin Sensitization

EPA assessed the potential for 1,2-hexanediol to cause skin sensitization using the results of an OECD Guideline 429 LLNA study on mice (Reported to the ECHA database, 2003b). The negative findings in this study provide sufficient information to indicate 1,2-hexanediol has low concern for skin sensitization.

6.1.9 Respiratory Sensitization

Experimental data determined to be of adequate quality[36] on 1,2-hexanediol or closely-related analogs were not reasonably available for the assessment of respiratory sensitization potential. To model respiratory sensitization for 1,2-hexanediol, EPA used NAMs, such as the QSAR Toolbox, version 4.2 models[37] 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 1,2-hexanediol. The results from these NAMs and weight of the scientific evidence provide 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[38] on 1,2-hexanediol or closely related analogs 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

[36] 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.

[37] 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

[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."

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 1,2-hexanediol, 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 1,2-hexanediol.

6.1.11 Skin Irritation

EPA assessed available experimental data on skin irritation. An OECD Guideline 404 study on rabbits exposed to 1,2-hexanediol reported negative results for skin irritation (Reported to the ECHA database, 1981b). A patch test study on humans also reported negative results for skin irritation (Lee et al., 2011). These results provide sufficient information to indicate low concern for 1,2-hexanediol to cause skin irritation.

6.1.12 Eye Irritation

EPA assessed potential for eye irritation from exposure to 1,2-hexanediol. Rabbits exposed to 1,2-hexanediol for 24 hours exhibited moderate eye irritation. After the 24-hour exposure, the animals were observed for reversibility. The effects were reversible in 14 days for corneal irritation, 7 days for iris irritation, and 10 days for conjunctivae irritation (Reported to the ECHA database, 1998a). These results indicate moderate to high concern for eye irritation (with reversible effects) by 1,2-hexanediol. The weight of scientific evidence for these results is discussed in Section 8.1.

6.1.13 Hazards to Potentially Exposed or Susceptible Subpopulations

The above information supports a low human health hazard finding for 1,2-hexanediol 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 1,2-hexanediol.

6.2 Environmental Hazard

To review environmental hazard endpoints without adequate quality[22] 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 and form the basis for designation. EPA assessed environmental hazard for 1,2-hexanediol based on available data on 1,2-hexanediol and closely-related analogs described above. EPA estimated chronic toxicity values using the Ecological Structure Active Relationships (ECOSAR) Predictive Model[39] and available experimental data. Appendix B contains a summary of the reasonably available environmental hazard data.

[39] https://www.epa.gov/tsca-screening-tools/ecological-structure-activity-relationships-ecosar-predictive-model

6.2.1 Acute Aquatic Toxicity

EPA assessed environmental hazard from acute exposures to 1,2-hexanediol based on available experimental data. Two studies evaluated the effects of acute exposure of 1,2-hexanediol to aquatic invertebrates. Both studies reported no mortality at the highest dose (100 mg/L), resulting in EC_{50}s greater than 100 mg/L (Lee et al., 2017; Reported to the ECHA database, 2012). For algal toxicity, *S. subspicatus* acutely exposed to pentylene glycol (Reported to the ECHA database, 1990) and 1,2-butanediol (Reported to the ECHA database, 1991) indicated very low concern, with EC_{50}s ranging from 500-9334 mg/L. However, another species of algae, *P. subcapitata,* exposed to 1,2-octanediol resulted in an EC50 of 35 mg/L (Reported to the ECHA database, 2007). Aquatic vertebrates acutely exposed to pentylene glycol indicated low concern with an LC_{50} greater than 1096 mg/L (Reported to the ECHA database, 1994). A chemical with acute aquatic toxicity values >10 ppm and <100 ppm is considered low concern for hazard if the chemical reaches a benchmark level of biodegradation (typically 60%) within 28 days as measured in a ready biodegradation test without degradation products of concern. Given the low persistence of 1,2-hexanediol (see Section 6.3.1, below), these aquatic toxicity results provide sufficient information to indicate low concern for acute aquatic exposure by exceeding the low-concern benchmark of 10 mg/L and demonstrating greater than 60% biodegradation within 28 days.

6.2.2 Chronic Aquatic Toxicity

EPA assessed environmental hazard from chronic exposures to 1,2-hexanediol based on available experimental data and estimated values using ECOSAR. Aquatic invertebrates chronically exposed to 1,2-hexanediol showed no mortality at the highest dose (10 mg/L), resulting in a no observed effect concentration (NOEC) of 10 mg/L (Lee et al., 2017). Toxicity from chronic exposures were estimated by ECOSAR using the neutral organics chemical class to occur at 66 mg/L for algae and 120 mg/L for aquatic vertebrates. These results provide sufficient information to indicate 1,2-hexanediol has low environmental hazard based on the low-concern chronic aquatic toxicity benchmark of 10 mg/L.

6.3 Persistence and Bioaccumulation Potential

6.3.1 Persistence

EPA assessed environmental persistence for 1,2-hexanediol. An experimental OECD Guideline 301B biodegradation study demonstrated this substance aerobically biodegraded by greater than 60 percent in 28 days, confirming it is readily biodegradable in a sewage sludge inoculum (Reported to the ECHA database, 1997). Given the aquatic toxicity values for this chemical, the low-concern benchmarks require that 1,2-hexanediol not produce degradation products of concern and readily biodegrade within 28 days.

EPA also assessed the potential for anaerobic biodegradation using read-across predictions from 1,2-octanediol. An OECD Guideline 311 indicated the analog anaerobically biodegraded by 68% in 60 days, indicating 1,2-hexanediol will biodegrade in anaerobic environments (Reported to the ECHA database, 2008).

No degradation products of concern were identified for this chemical substance. The available biodegradation results meet the low-concern benchmark and provide sufficient information to indicate this chemical will have low persistence.

6.3.2 Bioaccumulation Potential

Based on the estimated bioaccumulation factor (BAF) value of 1.1, using Estimation Programs Interface (EPI) Suite models,[40] EPA has sufficient information that 1,2-hexanediol has low potential for bioaccumulation in the environment based on the low-concern benchmark of less than 1000.

[40] https://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface

7. Exposure Characterization

EPA considered reasonably available information on exposure for 1,2-hexanediol. In general, there is limited information on exposure for low-hazard chemicals. EPA consulted sources of use information that include CDR database and other databases and public sources. Of these sources, EPA determined that the CDR database contained the primary source of information on the conditions of use for this exposure characterization. EPA used these sources (described in Table A.2) 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, 1,2-hexanediol is a solvent used in processing (incorporation into an article and into a formulation, mixture, or product) in the industrial printing ink manufacturing sector; as well as in ink, toner, and colorant products for consumer and commercial use (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 1,2-hexanediol is based on an analysis of CDR data reported from 1998 to 2016.[41] The CDR database indicates that, for reporting year 2015, three companies manufactured or imported 1,2-hexanediol at three sites. In 1998 and 2002 reporting years, aggregate production volume for 1,2-hexanediol was between 10,000 and 500,000 lbs., and in 2006 aggregate production volume was less than 500,000 lbs. The exact amount is available for one year, 2011, in which 94,095 lbs. of 1,2-hexanediol was produced or imported. Between 2012 and 2015, volume ranged between 25,000 and 500,000 lbs. Aggregate production volumes for each reporting year are provided in Table A.1.

7.2 Exposures to the Environment

EPA expects most exposures to the environment to occur during the processing of 1,2-hexanediol, specifically, the formulation of printing inks and toners. Exposure is also possible from other uses, such as manufacturing, distribution, consumer and commercial use, and disposal. These activities could result in releases of 1,2-hexanediol to media including surface water, landfills, and air.

EPA expects high levels of removal of 1,2-hexanediol 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). Further, 1,2-hexanediol has low persistence (aerobic and anaerobic biodegradation are discussed in Section 6.3.1) and has the potential to break down in the environment into carbon dioxide and water. Therefore, any release of this chemical is expected to

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

break down, reducing exposure to aquatic organisms in the water column, benthic organisms, and groundwater sources of drinking water, including well water.

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

If incineration releases during manufacturing and processing occur, EPA expects significant degradation of 1,2-hexanediol 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 1,2-hexanediol from the potential environmental releases described above. Air exposure is unlikely from incineration. If 1,2-hexanediol is present in the air from volatilization, it is expected to be reduced because of its short atmospheric half-life of 6.9 hours (see Table 2 in Section 3). 1,2-Hexanediol is unlikely to be present in surface water because of its degradation (aerobic and anaerobic biodegradation are discussed in Section 6.3.1), reducing the potential for the general population to be exposed by oral ingestion or dermal exposure. Given the low bioaccumulation or bioconcentration potential of 1,2-hexanediol, oral exposure to 1,2-hexanediol 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 1,2-hexanediol than the general population during manufacturing, processing, distribution, use, and disposal. EPA also identified consumers as a population that may experience greater exposure to 1,2-hexanediol than the general population through use of ink, toner, and colorant products.

7.4.1 Exposures to Workers

Based on its reported physical form and measured melting point (Table 2), 1,2-hexanediol is a liquid under ambient conditions. Based on 1,2-hexanediol'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 measured vapor pressure (Table 2), 1,2-hexanediol is expected to be volatile at ambient temperatures, and therefore workers may be exposed through inhalation of vapors. However, if 1,2-hexanediol is in a dilute form, the estimated Henry's Law constant for 1,2-hexanediol indicates volatilization from water and aqueous solutions is expected to be minimal. Workers may be exposed to 1,2-hexanediol in manufacturing, processing, distribution, use, and disposal.

7.4.2 Exposures to Consumers

Consumers could be exposed to 1,2-hexanediol through the use of ink, toner, and colorant products. Consumer exposure could occur through dermal contact with ink printed on products or in initial installation of a printer cartridge or toner. If dermal contact does occur, 1,2-hexanediol is expected to be moderately absorbed through the skin. 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). 1,2-hexanediol is expected to 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 1,2-hexanediol against each of the priority designation considerations in 40 CFR 702.9(a), and 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 and 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 1,2-hexanediol. EPA used this information to inform its determination of whether 1,2-hexanediol meets the statutory criteria and considerations for final designation as a low-priority substance.

- **Hazard potential:**

For 1,2-hexanediol'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 1,2-hexanediol is of low concern for human health and environmental hazard across the range of endpoints in these low-concern criteria except for eye irritation (see the discussion below).

- **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 1,2-hexanediol, exposure by dermal, inhalation and ingestion pathways are reduced by metabolism and excretion (discussed in Section 6.1.1). If 1,2-hexanediol is released into the environment, its exposure potential will be reduced through biodegradation under aerobic and anaerobic conditions.

Rationale: Although 1,2-hexanediol may have potential to cause moderate to high eye irritation, the effects are reversible, reducing concern for longer-term effects. TSCA conditions of use would be unlikely to result in frequent eye exposure because use patterns do not involve intentional eye exposure. Workers could be exposed during processing, manufacturing, distribution, use, and disposal, splashing of solutions, or hand-to-face and eye contact. Other uses covered under TSCA, especially consumer uses in products such as ink, toner, and colorant products, would be unlikely to result in more than incidental eye exposure. Eye irritation resulting from exposure in an occupational and consumer setting is mitigated by the reversible nature of the effect and furthermore by the strong likelihood that any exposures would be self-limiting, especially by those who experience eye irritation from eye exposure.

Conclusion: Based on 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 1,2-hexanediol meets the standard for a high-priority substance. The reasonably available hazard and exposure information described above provides sufficient information to support this finding. Even if the unlikely, infrequent, and temporary occurrence of potential moderate to high eye irritation were to occur, EPA does not find that this potential eye irritation rises to the significance of the standard for a high-priority substance (i.e., that the substance "may present an unreasonable risk of injury to health").

8.2 Persistence and Bioaccumulation

Approach: EPA has evaluated both the persistence and bioaccumulation potential of 1,2-hexanediol based on a set of EPA and internationally accepted measurement tools and benchmarks that are 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 1,2-hexanediol is readily biodegradable under aerobic conditions, with greater than 60 percent biodegradation within 28 days, and is expected to be biodegradable under anaerobic conditions with 68% biodegradation in 60 days based on a closely-related analog. EPA's EPI Suite models indicate a low potential for bioaccumulation and bioconcentration.

Conclusion: Based on an analysis 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 1,2-hexanediol 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 a 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 1,2-hexanediol as a potentially exposed or susceptible subpopulation. Consumers are also a potentially exposed subpopulation because of their use of products such as ink, toner, and colorant products (described in more detail in Section 7).

Rationale: EPA expects workers and consumers to have a higher exposure to 1,2-hexanediol than the general population. Because of the chemical's low-concern hazard properties and reversibility of the effects, this 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 1,2-hexanediol 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-hazard profile of 1,2-hexanediol 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 1,2-hexanediol 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. The 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, 1,2-hexanediol is expected to present low concern to the general population, including susceptible subpopulations, across a spectrum of health endpoints.

In the event of an accidental release into a surface drinking water source, 1,2-hexanediol is expected to be water soluble (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 highly mobile in soils, increasing its potential for leaching into groundwater, including well water. The fate and transport evaluation indicates 1,2-hexanediol is unlikely to partition into sediment, predicted to biodegrade under aerobic and anaerobic conditions (see Section 3), and unlikely to bioaccumulate (see Section 6), minimizing the likelihood that the chemical would be present in sediment or groundwater to 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, 1,2-hexanediol would degrade in aerobic and anaerobic 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.

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 1,2-hexanediol 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 1,2-hexanediol under 40 CFR 702.9(a)(4) does not support a finding that 1,2-hexanediol 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 1,2-hexanediol and related potential exposures and hazards.

Rationale: EPA evaluated the conditions of use of 1,2-hexanediol (see Section 5 and Appendix A) and found it to have a small range of conditions of use. EPA expects that even if the conditions of use were to expand beyond activities that are 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 1,2-hexanediol'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 1,2-hexanediol 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 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 1,2-hexanediol 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 1,2-hexanediol (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 1,2-hexanediol as a low-priority substance could result in increased use and higher production volumes. EPA expects, however, that any changes in 1,2-hexanediol'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 1,2-hexanediol'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 the 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 exposure, 1,2-hexanediol 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 1,2-hexanediol 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 1,2-hexanediol 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 1,2-hexanediol 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 lbs. per site per year. According to the 2016 CDR database, three companies manufactured or imported 1,2-hexanediol for reporting year 2015. Individual production volumes were withheld by EPA to protect against disclosure of CBI.

Table presents the historic production volume of 1,2-hexanediol from the CDR from 1986-2015. Prior to 1994, 1,2-hexanediol 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 1998 and 2002 reporting years, aggregate production volume for 1,2-hexanediol was between 10,000 and 500,000 lbs., and in 2006 aggregate production volume was less than 500,000 lbs. The exact amount is available for one year, 2011, in which 94,095 lbs. of 1,2-hexanediol was produced or imported. Between 2012 and 2015, volume ranged between 5,000 and 500,000 lbs. In general, since 1998, production volume has remained relatively stable without significant increases or decreases.

Table A.1: 1986-2015 National Production Volume Data for 1,2-Hexanediol (Non-Confidential Production Volume in Pounds)

1986	1990	1994	1998	2002	2006	2011	2012	2013	2014	2015
NDR	NDR	NDR	10 K – 500 K	10 K – 500 K	< 500 K	94,095	25K – <100K	100K- <500K	100K- <500K	25K- <100K

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

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

A.2 Uses

A.2.1 Methods for Uses Table

Section A.2.2 provides a list of known uses of 1,2-hexanediol, organized by category of use. To compile the uses, EPA searched publicly available databases listed in Table 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 1,2-Hexanediol

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)	6920-22-5; 1,2-hexanediol	No
Canada Chemicals Management Plan information sheets	Government of Canada (2018)	1,2-hexanediol	No
Chemical and Product Categories (CPCat)	CPCat (2019)	6920-22-5	Yes
ChemView [2]	EPA (2018)	6920-22-5	Yes
Children's Safe Product Act Reported Data	Washington State Dept. of Ecology (2018)	6920-22-5	No
Consumer Product Information Database (CPID)	DeLima Associates (2018)	6920-22-5	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)	1,2-hexanediol	No
DrugBank	DrugBank (2018)	6920-22-5	Yes
European Chemicals Agency (ECHA) Registration Dossier	EPA (2018)	6920-22-5	Yes
eChemPortal [2]	OECD (2018)	6920-22-5	Yes
Envirofacts [2]	EPA (2018)	6920-22-5; 1,2-hexanediol	No
Functional Use Database (FUse)	EPA (2017)	6920-22-5	Yes
Kirk-Othmer Encyclopedia of Chemical Technology	Kirk-Othmer (2006)	1,2-hexanediol; hexanediol	No
Non-Confidential 2016 Chemical Data Reporting (CDR)	EPA (2017)	6920-22-5	Yes
PubChem Compound	Kim et al. (2016)	6920-22-5	Yes
Safer Chemical Ingredients List (SCIL)	EPA (2018)	6920-22-5	Yes
Synapse Information Resources [2]	Synapse Information Resources (n.d.)	1,2-hexanediol	No

Table A.2: Sources Searched for Uses of 1,2-Hexanediol			
Title	**Author and Year**	**Search Term(s)**	**Found Use Information?** [1]
Resource Conservation and Recovery Act (RCRA)	EPA (2017)	1,2-hexanediol; hexanediol; hexane; 1,2	No
Scorecard: The Pollution Information Site	GoodGuide (2011)	6920-22-5; 1,2-hexanediol; 1,2-hex; DL-hexane	No
Skin Deep Cosmetics Database	EWG (2018)	6920-22-5	Yes
Toxics Release Inventory (TRI)	EPA (2018)	6920-22-5	No
TOXNET [2]	NLM (2018)	6920-22-5	Yes
Ullmann's Encyclopedia of Industrial Chemistry	Ullmann's (2000)	1,2-hexanediol; hexanediol	Yes
Additional Sources Identified from Reasonably Available			
Danish Environmental Protection Agency (Danish EPA)	Danish EPA (2015)	Incidentally identified while researching details of this chemical's uses and products.	Yes
Expanscience Laboratories	Expanscience Laboratoires (2017)		
Food-grade antimicrobials potentiate the antibacterial activity of 1,2-hexanediol	Yogiara et al. (2015)		
International Fragrance Association (IFRA)	IFRA (2016)		
National Pesticide Information Retrieval System (NPIRS)	National Pesticide Information Retrieval System (2016)		
Nature Republic	Nature Republic (2018)		
Xerox Corporation	Xerox Corporation (2018a)		

Note(s):
1. If use information was found in the resource, it will appear in Table 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 3,079 patents referencing "1,2-hexanediol" (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 1,2-hexanediol were not included in Table . Note that the uses in Table A.2 that are covered under TSCA are included in Section 5, Table 3 of this document.

A.2.2 Uses of 1,2-Hexanediol

Table A.3: Uses of 1,2-Hexanediol		
Use		**Description of Use and References**
TSCA Conditions of Use: Ink, Toner, and Colorant Products According to the 2016 CDR, 1,2-hexanediol is a solvent used in processing (incorporation into article, and incorporation into formulation, mixture, or product) in the industrial printing ink manufacturing sector; as well as in ink, toner, and colorant products for consumer and commercial use (EPA 2017b).		
Ink used in textiles, leather, and fur	Commercial	Reported to the ECHA database, 2018 The ECHA registration dossier indicates that 1,2-hexanediol has been used in commercial inks, the end use of which is reported as manufacture of textiles, leather, and fur. 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 commercial due to ECHA's inclusion as a use by professional workers.
Printing ink	Consumer, commercial, industrial	Xerox Corporation (2018a, 2018b); EPA (2017b); Ullmann's (2012) 1,2-Hexanediol was reported to be used in printing ink manufacturing and ink, toner, and colorant products in the 2016 CDR. A few current SDSs for printer ink containing 1,2-hexanediol were also available online. CDR indicates that the chemical functions as a solvent in this sector. CDR identified consumer and commercial use in "ink, toner, and colorant" products, and industrial use in printing ink manufacturing.
Toner	Consumer, commercial	EPA (2017b) 1,2-Hexanediol was reported to be used in ink, toner, and colorant products in the 2016 CDR. No examples of toner products confirmed to contain the chemical could be found. The functional use of the chemical in toners is unknown. CDR identified consumer and commercial use in "ink, toner, and colorant" products.
Other TSCA Uses		
Fuel and lubricant additive	Consumer, commercial, industrial	Ullmann's (2012) Ullmann's Encyclopedia reports 1,2-hexanediol as being used in fuel and lubricant additives. This use was not reported in the most recent CDR and no additional information on the chemical's use as a fuel or lubricant additive could be found. Fuel and lubricant additives are available for consumer, commercial, and industrial use, depending on their application. Due to limited available information, EPA has not confirmed any of these expected users.

Table A.3: Uses of 1,2-Hexanediol		
Use		**Description of Use and References**
Non-TSCA Uses		
Acne treatment	Consumer	EWG (2018) EWG previously listed an acne treatment product in the Skin Deep database that contained 1,2-hexanediol but the product has since been removed. It is unknown whether other current acne products contain the chemical.
After shave	Consumer	EWG (2018)
Anti-aging cream and liquid	Consumer	DeLima Associates (2015c, 2009, 2008); EWG (2018) EWG's Skin Deep and CPID generally include products for consumer use; therefore, the expected user is a consumer.
Baby lotion	Consumer	EWG (2018)
Baby soap	Consumer	EWG (2018) .
Baby wipes	Consumer	EWG (2018)
Beauty-related eye product	Consumer	Nature Republic (2018); DeLima Associates (2015a, 2015b, 2015c) This use category includes eye creams, mascara, depuffers, and anti-aging products. The functional use of 1,2-hexanediol in these products is unknown.
Blush	Consumer	EWG (2018)

Table A.3: Uses of 1,2-Hexanediol		
Use		**Description of Use and References**
Body soap (liquid)	Consumer	DeLima Associates (2016b); EWG (2018)
Body soap	Consumer	DeLima Associates (2015a); EWG (2018)
Bronzer	Consumer	EWG (2018) The bronzer product reported by EWG no longer contains 1,2-hexanediol according to the ingredients listed on the company's website. However, it is possible that other bronzers still contain the chemical.
Concealer	Consumer	EWG (2018)
Conditioner	Consumer	EWG (2018)
Disinfectant	Industrial	Reported to the ECHA database, 2018; National Pesticide Information Retrieval System (2016) The ECHA registration dossier indicates that 1,2-hexanediol has been used in biocidal (e.g., disinfectant; pest control) products. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. The National Pesticide Information Retrieval system indicates that no federally active pesticide products contain 1,2-hexanediol. Expected users are industrial due to ECHA's inclusion as a use at industrial sites.
Exfoliant scrub	Consumer	EWG (2018)
Eye liner	Consumer	EWG (2018)

Table A.3: Uses of 1,2-Hexanediol		
Use		**Description of Use and References**
Eye shadow	Consumer	EWG (2018)
Face mask	Consumer	EWG (2018); DrugBank (2018)
Facial soap	Consumer	CPCat (2019); EWG (2018)
Foundation	Consumer	EWG (2018)
Fragrance	Unknown	IFRA (2016); Danish EPA (2015) The International Fragrance Association (IFRA) reported the use of 1,2-hexanediol as a fragrance compound in 2015. The list does not specify the country of use or manufacture. One currently available fragrance product containing the chemical was identified, but it is unknown whether the function of 1,2-hexanediol in the product is as a fragrance itself, or if it is serving another function. The expected users are unknown, due to the limited availability of information.
Hair spray	Consumer	DeLima Associates (2016a, 2015d); EWG (2018)
Hair styling gel	Consumer	EWG (2018)
Lip gloss, lip balm, and lipstick	Consumer	CPCat (2019); EWG (2018)
Makeup primer	Consumer	EWG (2018)

Table A.3: Uses of 1,2-Hexanediol		
Use		**Description of Use and References**
Makeup remover	Consumer	EWG (2018)
Moisturizer	Consumer	CPCat (2019); EWG (2018)
Nail polish	Consumer	EWG (2018)
Perfume	Consumer	EWG (2018); Expanscience Laboratoires (2017) EWG's Skin Deep included a perfume spray product containing 1,2-hexanediol. It is unknown whether the chemical is used for its fragrance or some other functional use within the product. Expected users are consumer, based on the one identified fragrance product sold to consumers. The product's website indicates that it can be used for babies.
Pharmaceutical	Consumer, commercial	Reported to the ECHA database, 2018 The ECHA registration dossier indicates that 1,2-hexanediol has been used in cosmetic and pharmaceutical products. 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 and commercial due to ECHA's inclusion as a professional use and consumer use.
Shampoo	Consumer	EWG (2018)
Shaving cream	Consumer	EWG (2018)
Sunscreen	Consumer	EWG (2018)

Table A.3: Uses of 1,2-Hexanediol		
Use		**Description of Use and References**
Tanning oil	Consumer	EWG (2018)
Children's Products CDR reports did not include any uses in children's products; however, uses in baby lotion, baby wipes, baby soap, and one perfume product intended for babies are found in this table.		
Recycling and Disposal In the 2016 CDR, two facilities reported that 1,2-hexanediol was not recycled (e.g., not recycled, remanufactured, reprocessed, or reused). One facility reported this information as CBI (EPA 2017b).		

A.3 References

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Appendix B: Hazard Characterization

Table B.1: Human Health Hazard

Acute Mammalian Toxicity

Source (HERO ID)	Exposure Route	Species & Strain (if available)	Duration	Doses and Replicate Number	Effect	Study Details
4729532	Oral (gavage)	Sprague-Dawley Rats	Single dose, 14 day observation period	**Doses and respective replicate information:** • 2043 mg/kg:3M, No F • 4408 mg/kg: 5M, 5F • 5339 mg/kg: 5M, 5F • 6470 mg/kg: 5M, 5F • 7338 mg/kg: 5M, 10F • 9500 mg/kg: 10F, no M	**LD_{50}**: • Males: Between 6166 mg/kg and 7338 mg/kg • Females: Between 5339 mg/kg and 9500 mg/kg	**Methods:** • Test substance reported as CASRN 6920-22-5 • Purity not reported • OECD Guideline 401 study (Acute oral toxicity) • GLP compliance not reported
5076436	Inhalation (aerosol)	Tif:Ralf (SPF) Rats	4 hours, 14-day observation period	**Doses:** 3.38 mg/L and 7.015 mg/L **Replicates:** 10 per sex per group	**LC_{50}** > 7.015 mg/L	**Methods:** • Test substance reported as CASRN 5343-92-0 • Purity not reported • OECD Guideline 403 study (Acute inhalation toxicity) • Not GLP compliant
5076431	Dermal	Tif:Ralf (SPF) Rats	24 hours, 14-day observation period	**Dose:** 2000 mg/kg **Replicates:** 5 per sex	**LD_{50}** > 2000 mg/kg	**Methods:** • Test substance reported as CASRN 5343-92-0 • Purity not reported • OECD Guideline 402 study (Acute dermal toxicity) • Not GLP compliant

Table B.1: Human Health Hazard						
Repeated Dose Toxicity						
Source (HERO ID)	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and Replicate number**	**Effect**	**Study Details**
4729540	Dermal	Sprague-Dawley Rats	91-93 days	**Doses:** 0, 350, 700, 1000 mg/kg-day **Replicates:** 15 rats per sex per group	**NOAEL:** 700 mg/kg-day **LOAEL:** 1000 mg/kg-day based on reduced body weight gain in males and females and increased total leukocyte count and urinary protein in females.	**Methods:** • Test substance reported as CASRN 6920-22-5 • Purity not reported • OECD Guideline 411 • GLP compliant
5353269	Oral (gavage)	Wister Rats	91-92 days	**Doses:** 0, 50, 250, 1000 mg/kg-day **Replicates:** 10 per sex per group	**NOAEL:** 1000 mg/kg-day	**Methods:** • Test substance reported as CASRN 5343-92-0 • Purity: 99.7% • OECD Guideline 408 • GLP compliant
5353268	Oral (gavage)	Wister Rats	28 days	**Doses:** 0, 50, 300, 1000 mg/kg-day **Replicates:** 5 per sex per group	**NOAEL:** 300 mg/kg-day; **LOAEL:** 1000 mg/kg-day based on reduced locomotor activity, and changes in organ weight	**Methods:** • Test substance reported as CASRN 1117-86-8 • Purity >98% • OECD Guideline 407 • GLP compliant **Results:** • Kidney weights in both sexes and liver weights in males were slightly higher than controls

Table B.1: Human Health Hazard						
Reproductive Toxicity						
Source (HERO ID)	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and Replicate Number**	**Effect**	
4729567	Dermal	Sprague-Dawley Rats	91-93 days	**Doses:** 0, 350, 700, or 1000 mg/kg-day **Replicates:** 15 per sex per group	**NOAEL**: 1000 mg/kg-day	**Methods** • Test Substance reported as CASRN 6920-22-5 • Purity not reported • OECD Guideline 411 • GLP compliant
Developmental Toxicity						
Source (HERO ID)	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and Replicate Number**	**Effect**	**Study Details**
3038919, 4729568	Oral (gavage)	Sprague-Dawley Rat; CD strain	Gestational day 5-19	**Doses**: 0, 30, 100, & 300 mg/kg-day **Replicates:** 24 pregnant rats per group	**NOAEL** (maternal and development): 300 mg/kg-day	**Methods:** • Test substance reported as CASRN 6920-22-5 • 99% purity • OECD Guideline 414 study • GLP compliant
4729569	Oral (gavage)	Sprague-Dawley Rats	Gestational day 6-19	**Doses**: 0, 250, 500, 750 mg/kg-day **Replicates:** 25 per dose	**Maternal** **NOAEL**: 500 mg/kg-day **LOAEL**: 750 mg/kg-day based on decreased body weight and decreased absolute and relative feed consumption **Developmental** **NOAEL:** 750 mg/kg-day	**Methods:** • Test substance reported as CASRN 6920-22-5 • Purity not reported • OECD Guideline 414 study (Prenatal Developmental Toxicity Study) • GLP compliant

Table B.1: Human Health Hazard		
Cancer		
Source	**Effect**	**Study Details**
Oncologic 8.0	Oncologic currently has no assessment criteria regarding diols.	**Results:** Structure could not be evaluated by Oncologic.
ISS v2.4[42]	Negative (Estimated) 1,2-Hexanediol is an aliphatic diol which does not contain any structural features indicative of electrophilic potential. It is rapidly metabolized through oxidation and glucuronidation.	**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 (an aldehyde alert was identified for the initial aldehyde metabolite that is formed in the first oxidation transformation that occurs during the metabolism of 1,2-hexanediol). This aldehyde will be rapidly transformed to the corresponding carboxylic acid (see Figure 6 metabolic tree in Metabolic Pathway Trees Supplemental Document[43]).
VEGA 1.1.4[44]	1,2-Hexanediol was processed through all 4 models. IRFMN/ISSCAN-GX 1.0.0 predicted it to be non-carcinogenic with moderate reliability.[45]	**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 (1,2-hexanediol lies outside of the applicability domain (AD) of the model) • ISS 1.0.2: Low reliability (1,2-hexanediol lies outside of the AD) • IRFMN/Antares 1.0.0: Low reliability (1,2-hexanediol lies outside of the AD) • IRFMN/ISSCAN-GX 1.0.0: Moderate reliability (1,2-hexanediol could be outside of the AD)

[42] 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).

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

[44] 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						
Genotoxicity						
Source (HERO ID)	**Test Type & Endpoint**	**Species & Strain (if available)**	**Metabolic Activation**	**Doses and Controls**	**Results**	**Study Details**
4729541	Gene mutation *(In vitro)*	E. coli WP2 uvr A pKM 101	With and without	**Doses:** 0, 25, 75, 200, 600, 1800, and 5000 µg/plate	Negative both with and without metabolic activation	**Methods:** • Test substance reported as CASRN 6920-22-5 • Purity not reported • OECD Guideline 471 study (Bacterial Mutation Assay) • GLP compliant
4729541	Gene mutation *(In vitro)*	Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538	With and without	**Doses:** 0, 25, 75, 200, 600, 1800, and 5000 µg/plate	Negative both with and without metabolic activation	**Methods:** • Test substance reported as CASRN 6920-22-5 • Purity not reported • GLP compliance not reported **Results:** • Cytotoxicity observed at 5000 µg/plate.
4729566	Gene mutation *(In vitro)*	Chinese hamster lung fibroblasts V79	With and without	**Doses:** 36.94,73.88, 147.75, 295.5, 591 and 1182 µg/mL	Negative both with and without metabolic activation	**Methods:** • Test substance reported as CASRN 6920-22-5 • Purity: 99.6% • OECD Guideline 476 study (*In vitro* mammalian cell gene mutation test) • GLP compliant **Results:** • No cytotoxicity
4729542	Chromosomal aberrations *(In vitro)*	Chinese hamster ovary cell	With and without	**Doses:** 148, 295, 590, and 1180 ug/mL	Negative both with and without metabolic activation	**Methods:** • Test substance reported as CASRN 6920-22-5 • Purity not reported

[45] Each model is characterized by an applicability domain (AD) that depends on at least 5 components:

- Similar substances with known experimental values within the underlying training set
- Accuracy of prediction for similar substances
- Concordance for similar substances,
- Fragments similarity check on the basis of atom centered fragments,
- Model descriptors range check.

A global AD index takes into account the other 5 components to provide an overall reliability score – low, moderate or high. EPA has not included low-reliability model results.

Table B.1: Human Health Hazard						
						• OECD Guideline 473 study (*In vitro* mammalian chromosome aberration test) • GLP compliant **Results:** • No cytotoxicity
Neurotoxicity						
Source (HERO ID)	**Exposure Route**	**Species & strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
5353269	Oral (gavage)	Wister Rats	91-92 days	**Doses:** 0, 50, 250, and 1000 mg/kg-day **Replicates:** 10 per sex per group	**NOAEL:** 1000 mg/kg-day	**Methods:** • Test substance reported as CASRN 5343-92-0 • Purity: 99.7% • OECD Guideline 408 • GLP compliant
5353268	Oral (gavage)	Wister Rats	28 days	**Doses:** 0, 50, 300, and 1000 mg/kg-day **Replicates:** 5 per sex per group	**NOAEL:** 300 mg/kg-day **LOAEL:** 1000 mg/kg-day based on reduced locomotor activity	**Methods:** • Test substance reported as CASRN 1117-86-8 • Purity >98% • OECD Guideline 407 • GLP compliant **Results:** • Slight reduction in locomotor activity in 1000 mg/kg group • No effects on histopathology of the brain, spinal cord or sciatic nerve
Sensitization						
Source (HERO ID)	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and Replicate Number**	**Effect**	**Study Details**
4729535	Skin	Female CBA mice	3 consecutive days	**Dose**: 0.25 µl at concentrations of 10, 50, and 100% **Replicates**: 5 animals per dose	Negative	**Methods:** • Test substance reported as CASRN 6920-22-5 • Purity not reported • OECD Guideline 429 study (LLNA), OECD Guideline 406 principles • GLP compliant **Results:** • Stimulation index < 3

Table B.1: Human Health Hazard						
Irritation						
Source (HERO ID)	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses**	**Effect**	**Study Details**
4729533	Skin	Russian Albino rabbit	4 hours	**Dose:** 0.5 mL **Replicates**: 3 per sex	Negative	**Methods:** • Test substance reported as CASRN 6920-22-5 • Purity >97% • OECD Guideline 404 study (Acute Dermal Irritation/Corrosion) • GLP compliance not reported
4674233	Skin	Human	24 hours	**Dose:** 20 µL **Replicates:** 38 Females, 1 Male	Negative	**Methods:** • Test substance reported as CASRN 6920-22-5 • Purity: 98% • Dose administered on filter paper to the skin • Patches evaluated at 30 minutes and 24 hours after patch removal • Erythema scored 0-4 **Results:** • Objective irritation score was <0.2/4
4729534	Eye	New Zealand white rabbit	24 hours	**Dose**: 10 µL **Replicates**:1 male, 2 females	Positive	**Methods:** • Test substance reported as CASRN 6920-22-5 • Purity not reported • Standard method for Evaluation of Eye Irritation in Albino Rabbits, E 1055-85, ASTM, OECD Guideline 405 • GLP compliant **Results:** • Cornea opacity: scored 2/4, but fully reversible by 14 day • Iris: scored ½ at 1, 24, 48hrs, and 0.67/2 at 72 hours, but fully reversible by 7 days

Table B.1: Human Health Hazard						
						• Conjunctivae: scored 2/3 at 1, 24 and 48hr and 1.3334 at 72 hours, but fully reversible within 10 day • Chemosis: 2/4 at 1,24, and 48 hours, 1.33/4 at 72 hours, but fully reversible within 10 day

Table B.2: Environmental Hazard					
Aquatic Toxicity: Experimental					
Source (HERO ID)	**Species & strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
5076435	*Scenedesmus subspicatus*	72 hours	**Doses:** 1500, 3000, 6000, 12000, 24000, and 48000 mg/L (nominal concentrations)	**EC_{50}:** 9334.69 mg/L	**Methods:** • Test substance reported as CASRN 5343-92-0 • Purity not reported • Test method: DIN 38412 Part 9 • Not GLP compliant
5076430	*Scenedesmus subspicatus*	72 hours	**Doses:** 0, 31.25, 62.5, 125, 250, and 500 mg/L (nominal concentrations)	**EC_{50}** > 500 mg/L	**Methods:** • Test substance reported as CASRN 584-03-2. • Purity not reported • Test method: DIN 38412 part 9 • Not GLP compliant
5076433	*Pseudokirchneriella subcapitata*	72 hours	**Doses:** 2, 5, 10, 20, 50, 100, 2and 00 mg/L (nominal concentrations)	**EC_{50}:** 35 mg/L	**Methods:** • Test substance reported as CASRN 1117-86-6 • Purity not reported • OECD Guideline 201 study (Freshwater algae and Cyanobacteria, Growth Inhibition Test) • GLP compliant.

Table B.2: Environmental Hazard					
3605033	*Daphnia magna*	48 hours	**Doses**: 0, 6.25, 12.5, 25, 50, and 100 mg/L (nominal concentrations)	**EC_{50}** > 100 mg/L	**Methods:** • Test substance reported as CASRN 6920-22-5 • Purity: 98% • OECD Guideline 202 (Acute immobilization test) • GLP compliance not reported
4729531	*Daphnia magna*	48 hours	**Dose:** 110 mg/L **Replicates:** 4 replicates	**EC_{50}** > 110 mg/L	**Methods:** • Test substance reported as CASRN 6920-22-5 • Purity not reported • OECD Guideline 202 study (Acute immobilization test) • GLP complaint
3605033	*Daphnia magna*	21 days	**Doses**: 0, 0.1, 0.3, 1.0, 3.2, and 10.0 mg/L (nominal concentrations); 0, 0.09, 0.29, 0.89, 2.96, and 9.05 mg/L (measured concentrations)	**NOEC:** 10 mg/L	**Methods:** • Test substance reported as CASRN 6920-22-5 • Purity: 98% • OECD Guideline 211 study (*Daphnia magna* Reproduction test) • GLP compliance not specified
5076429	*Danio rerio*	96 hours	**Doses:** 0, 48, 100, 183, 449, 1096 mg/L (measured concentrations)	**LC_{50}** > 1096 mg/L	**Methods:** • Test substance reported as CASRN 5343-92-0 • Purity: 99% • OECD Guideline 203 study (Fish, Acute toxicity test) • GLP compliant
Aquatic Toxicity: Estimated					
Model	**Chemical Class**	**Species**	**Predicted Effect Level**	**Notes**	
ECOSAR v2.0	Neutral organics	Green algae	96-hour EC_{50}: 330 mg/L	Physical properties used for estimation: WS 26171 mg/L (est), log K_{ow} 0.69 (est); SMILES: OCC(O)CCCC	
ECOSAR v2.0	Neutral organics	Fish	96-hour LC_{50}: 1450 mg/L	Physical properties used for estimation: WS 26171 mg/L (est), log K_{ow} 0.69 (est); SMILES: OCC(O)CCCC	

Table B.2: Environmental Hazard				
ECOSAR v2.0	Neutral organics	Fish	ChV: 120 mg/L	Physical properties used for estimation: WS 26171 mg/L (est), log K_{ow} 0.69 (est); SMILES: OCC(O)CCCC
ECSAR v2.0	Neutral organics	green algae	ChV: 66 mg/L	Physical properties used for estimation: WS 26171 mg/L (est), log K_{ow} 0.69 (est); SMILES: OCC(O)CCCC

Table B.3: Fate					
Environmental Fate: Experimental					
Source (HERO ID)	**Endpoint**	**Duration**	**Doses and number of replicates**	**Results**	**Study Details**
4729530	Environmental persistence	28 days	• Sludge: Activated, non-adapted sludge (2500 mg solids/L) • Chemical: 10 mg/L (based on TOC) • Two test replicates	• Replicate 1: 82.1% degradation in 28 days • Replicate 2: 83.7% degradation in 28 days • Test substance reported to be readily biodegradable	**Methods:** • Test substance reported as CASRN 6920-22-5 • Purity not reported • OECD Guideline 301B (CO_2 Evolution) • GLP compliant
5076434	Anaerobic biodegradation	60 days	• Test substance dose: 77.4 mg/L • Replicates: 8	• Ultimately anaerobically biodegradable	**Methods:** • Test substance reported as CASRN 1117-86-8 • Purity not reported • OECD Guideline 311 (Anaerobic Biodegradability of Organic Compounds in Digested Sludge) • GLP compliant • Sludge: Anaerobic digested sludge from a WWTP **Replicate average results:** • 0%/ 0 days; 5.4%/ 7 days; 11.4%/ 14 days; 16.3%/ 21 days; 41.7%/ 28 days; 59.0%/ 36 days; 63.2%/ 42 days; 65.2%/ 49 days; 67.3%/ 56 days

Table B.3: Fate				
Experimental Fate: Modelled				
Model	**Data Type**	**Endpoint**	**Predicted Endpoint**	**Notes**
EPISuite v4.11	Estimated	BCF	3.2	Experimental input value: log K_{ow}: 0.58
EPISuite v4.11	Estimated	BAF	1.1	Experimental input value: log K_{ow}: 0.58

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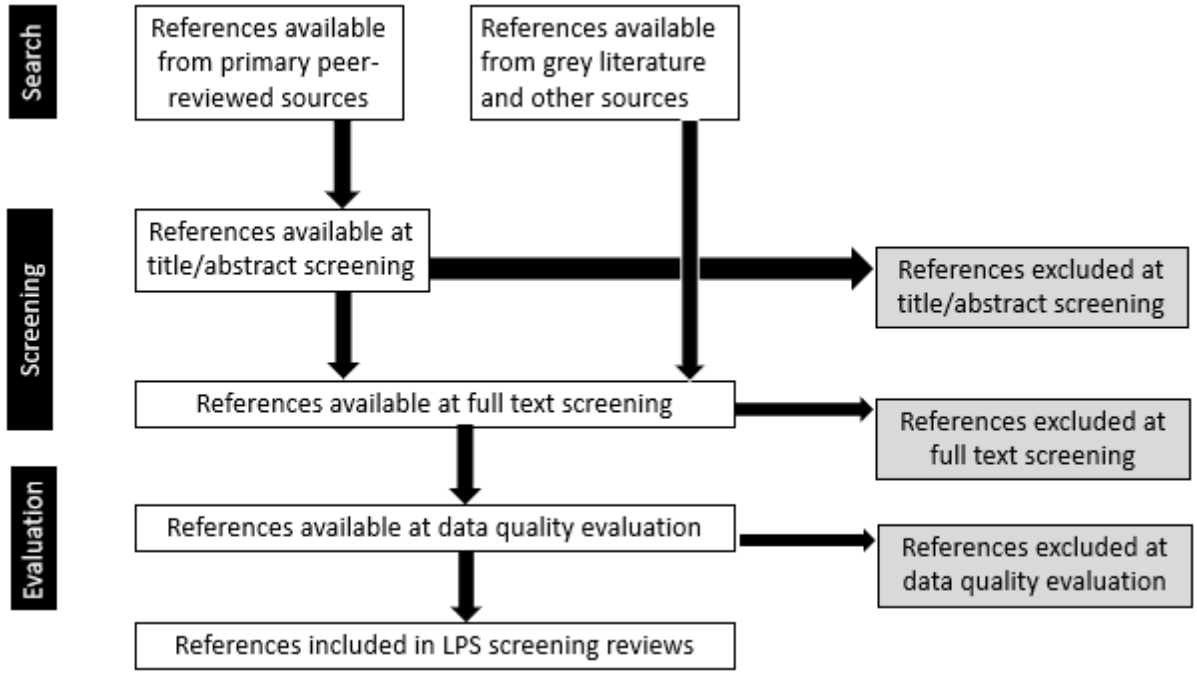
Appendix C: Literature Search Outcomes

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 1,2-hexanediol. Search outcomes and reference details are provided on the candidate's HERO[46] project page.

EPA created a fit-for-purpose process to transparently document the literature search and review[47] of available hazard and fate information for low-priority substance (LPS) candidates. References from peer-reviewed primary sources, grey sources,[48] 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



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

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

[48] 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 for Analog Data

To supplement the information on the candidate chemical, 1,2-hexanediol, the following analogs were identified:1,2-butanediol (CASRN 584-03-2), pentylene glycol (CASRN 5343-92-0), and 1,2-octanediol (CASRN 11117-86-8). For more details and justification on analogs, see section 6.1.1. Analogs were used to fill data gaps on endpoints for which 1,2-hexanediol lacked quality data, such neurotoxicity, or to add to the weight of the scientific evidence. EPA collected reasonably available information for these endpoints by searching specific grey literature and other secondary sources, listed on Table C.1. If information related to the identified analogs were available in these sources, the references were screened and evaluated using the same process as references on 1,2-hexanediol described above.[47]

Table C.1: Sources Used for Analog Search	
Resource	**URL**
ATSDR	http://www.atsdr.cdc.gov/toxprofiles/index.asp
ChemID (EPA – HPVIS via ChemID)	http://chem.sis.nlm.nih.gov/chemidplus/
CIR	http://www.cir-safety.org/ingredients
ECHA	http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances
ECOTOX	https://cfpub.epa.gov/ecotox/quick_query.htm
EPA – ChemView (incl. TSCATS, RBP/HC, and HPV/HPVIS)	https://chemview.epa.gov/chemview
European Food Safety Authority (EFSA)	http://www.efsa.europa.eu/
FDA	https://www.fda.gov/default.htm
HERA	http://www.heraproject.com/RiskAssessment.cfm
NICNAS	http://www.nicnas.gov.au/
NITE (J-CHECK)	http://www.safe.nite.go.jp/jcheck/search.action?request_locale=en
NTP	https://ntpsearch.niehs.nih.gov/home
OECD/SIDS	https://hpvchemicals.oecd.org/UI/Search.aspx; http://webnet.oecd.org/hpv/ui/SponsoredChemicals.aspx

C.1.2 Search Terms and Results

EPA began the literature review process for the hazard screening of 1,2-hexanediol 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.2 lists the search terms used in the database search of peer -reviewed literature for 1,2-hexanediol. For grey literature and other secondary sources, Table C.3 lists the search terms used for 1,2-hexanediol and analogs.

Table C.2: Search Terms Used in Peer Reviewed Databases		
Discipline	**Database**	**Search terms**[49]
Human Health	PubMed	6920-22-5[rn] OR "1,2-Dihydroxyhexane"[tw] OR "1,2-Hexanediol"[tw] OR "5,6-Dihydroxyhexane"[tw] OR "DL-1,2-Hexanediol"[tw] OR "DL-Hexane-1,2-diol"[tw]

[49] 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.2: Search Terms Used in Peer Reviewed Databases		
		OR "1,2-Hexyleneglycol"[tw] OR "DL-Hexan-1,2-diol"[tw] OR "DL-hexano-1,2-diol"[tw]
	Toxline	(6920-22-5 [rn] OR "1,2-Hexyleneglycol" OR "DL-Hexan-1,2-diol" OR "DL-hexano-1,2-diol" OR "1 2-dihydroxyhexane" OR "1 2-hexanediol" OR "5 6-dihydroxyhexane" OR "dl-1 2-hexanediol" OR "dl-hexane-1 2-diol") AND (ANEUPL [org] OR BIOSIS [org] OR CIS [org] OR DART [org] OR EMIC [org] OR EPIDEM [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]
	TSCATS 1	6920-22-5[rn]
	WOS	TS=("1,2-Hexyleneglycol" OR "DL-Hexan-1,2-diol" OR "DL-hexano-1,2-diol" OR "1,2-Dihydroxyhexane" OR "1,2-Hexanediol" OR "5,6-Dihydroxyhexane" OR "DL-1,2-Hexanediol" OR "DL-Hexane-1,2-diol")
Environmental Hazard	WOS	Same as human health strategy synonyms only
	Toxline	Same as human health strategy synonyms only
	TSCATS 1	Same as human health strategy CASRN only
	Proquest	"6920-22-5" OR "1,2-dihydroxyhexane" OR "1,2-hexanediol" OR "5,6-dihydroxyhexane" OR "dl-1,2-hexanediol" OR "dl-hexane-1,2-diol" OR "1,2-Hexyleneglycol" OR "DL-Hexan-1,2-diol" OR "DL-hexano-1,2-diol"
Fate	WOS	Same as human health strategy synonyms only

Table C.3: Search Terms Used in Grey Literature and Additional Sources	
Chemical	**Search terms**
1,2-Hexanediol	Searched as a string or individually depending on resource: "6920-22-5" OR "1,2-dihydroxyhexane" OR "1,2-hexanediol" OR "5,6-dihydroxyhexane" OR "dl-1,2-hexanediol" OR "dl-hexane-1,2-diol"
Analogs searched	pentylene glycol (5343-92-0); 1,2-butanediol (584-03-2); 1,2-octanediol (1117-86-8)

After the search terms were applied, more than 150 references were returned by all search efforts across peer-reviewed databases and grey literature sources. The total number of references include database results, additional strategies, and analog searches. All references from the search efforts were screened and evaluated through the LPS literature search and review process.[47] Of these, 18 references were included for data evaluation and used to support the designation of 1,2-hexanediol 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 1,2-hexanediol. 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[47] 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 1,2-hexanediol, EPA excluded a total of 108 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.4), or full-text screening (see Table C.5). Unacceptable references (e.g., studies that did not meet data quality metrics) were excluded at full-text screening (see Tables C.6 and C.7). Off-topic and unacceptable references are displayed next to the corresponding exclusion criteria.

Table C.4: Off-Topic References Excluded at Title/Abstract Screening for Human Health Hazard

Reference excluded (HERO ID) because the reference did NOT contain information needs[50] relevant to human health hazard									
1205485	3039332	4421783	4674224	4674238	4683976	4683986	4684012	4684044	4684079
1612136	3407162	4422636	4674225	4674239	4683977	4683987	4684016	4684045	4684080
1614234	4275027	4428186	4674228	4674889	4683979	4683988	4684019	4684046	4684083
1621555	4399677	4429336	4674229	4683772	4683980	4683993	4684021	4684047	4684086
1962870	4409714	4432999	4674230	4683774	4683981	4684004	4684038	4684048	
2044953	4410096	4670341	4674231	4683778	4683982	4684005	4684039	4684049	
2046206	4415908	4674220	4674232	4683782	4683983	4684006	4684040	4684061	
2960791	4419365	4674222	4674235	4683785	4683984	4684008	4684042	4684065	
3037506	4421781	4674223	4674237	4683975	4683985	4684011	4684043	4684067	
Reference excluded (HERO ID) because the reference primarily contained *in silico* data									
N/A.									

Table C.5: 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	N/A.
What type of source is this reference?	Review article or book chapter that contains only citations to primary literature sources	N/A.
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.

[50] 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.5: 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)**
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	4674226
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	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.
Does the paper report a negative control that is a vehicle control or no treatment control?	No[51]	N/A.
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	3037835 4674236 4684041 4684084
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	3037835 4674227 4674234 4674236 4683790 4684041 4684084
For genotoxicity studies only: Does the study use a positive control?	No	N/A.

[51] 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.6: 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.
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).	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., <28 days for repeat dose).	N/A.
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).	N/A.

Table C.6: 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 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.
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.).	N/A.
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.	N/A.

Table C.7: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Human Health Hazard – In Vitro		
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: Negative controls	A concurrent negative control group was not included or reported. **OR** The reported negative control group was not appropriate (e.g., different cell lines used for controls and test substance exposure).	N/A.

Table C.7: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Human Health Hazard – In Vitro		
Data Quality Metric	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 3: Positive controls	A concurrent positive control or proficiency group was not used.	N/A.
Metric 4: Assay type	The assay type was not reported. **OR** The assay type was not appropriate for the study type or outcome of interest (e.g., *in vitro* skin corrosion protocol used for *in vitro* skin irritation assay).	N/A.
Metric 5: Reporting of concentration	The exposure doses/concentrations or amounts of test substance were not reported.	N/A.
Metric 6: Exposure duration	No information on exposure duration(s) was reported. **OR** The exposure duration was not appropriate for the study type and/or outcome of interest (e.g., 24 hours exposure for bacterial reverse mutation test).	4674221
Metric 7: Metabolic activation	No information on the characterization and use of a metabolic activation system was reported. **OR** The exposure duration was not appropriate for the study type and/or outcome of interest (e.g., 24 hours exposure for bacterial reverse mutation test).	N/A.
Metric 8: Test model	The test model was not reported **OR** The test model was not routinely used for evaluation of the specific outcome of interest.	N/A.
Metric 9: Outcome assessment methodology	The outcome assessment methodology was not reported. **OR** The assessment methodology was not appropriate for the outcome(s) of interest (e.g., cells were evaluated for chromosomal aberrations immediately after exposure to the test substance instead of after post-exposure incubation period).	N/A.

C.2.2 Environmental Hazard

For the screening review of LPS candidate 1,2-hexanediol, EPA excluded a total of 109 references when assessing environmental hazard. Off-topic environmental hazard references excluded at title/abstract screening are listed in Table C.8, and those excluded at full-text screening are listed in Table C.9. References in Table C.10 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.8: Off-Topic References Excluded at Title/Abstract Screening for Environmental Hazard

Reference excluded (HERO ID) because the reference did NOT contain information needs[52] relevant to environmental hazard									
1205485	3039332	4422636	4674231	4683778	4683798	4683975	4683987	4684021	4684049
1612136	3407162	4428186	4674232	4683779	4683799	4683976	4683988	4684038	4684061
1614234	4072237	4429336	4674235	4683782	4683800	4683977	4683993	4684039	4684065
1621555	4275027	4432999	4674238	4683785	4683801	4683979	4684004	4684040	4684067
1962870	4399677	4670341	4674239	4683789	4683803	4683980	4684005	4684042	4684079
2044953	4409714	4674220	4674889	4683791	4683804	4683981	4684006	4684043	4684080
2046206	4410096	4674222	4683769	4683792	4683805	4683982	4684008	4684044	4684083
2283233	4415908	4674224	4683770	4683793	4683807	4683983	4684011	4684045	4684086
2960791	4419365	4674225	4683772	4683794	4683808	4683984	4684012	4684046	
2964776	4421781	4674228	4683774	4683795	4683809	4683985	4684016	4684047	
3037506	4421783	4674230	4683775	4683796	4683810	4683986	4684019	4684048	
Reference excluded (HERO ID) because the reference did NOT present quantitative environmental hazard data									
N/A.									

Table C.9: 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	4684031
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	No	N/A.

[52] 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.9: Screening Questions and Off-Topic References Excluded at Full-Text Screening for Environmental Hazard		
Question	**Off-topic if answer is:**	**References excluded (HERO ID)**
species (fish, invertebrates, microorganisms, non-mammalian terrestrial species)?		
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?	Mixture	N/A.
	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	5076432
Does the reference include endpoints in the information needs?	No	N/A.

Table C.10: 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	N/A.

Table C.10: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Environmental Hazard		
Question	**Unacceptable if:**	**References excluded (HERO ID)**
	organisms for an acceptable period of time prior to mating).	
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.
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 1,2-hexanediol EPA excluded a total of 84 references when assessing environmental fate. Off-topic fate references excluded at title/abstract screening are listed in Table C.11, and those excluded at full-text screening are listed in Table C.12. References in Table C.13 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.11: Off-Topic References Excluded at Initial Screening for Fate								
Reference excluded (HERO ID) because the reference did NOT contain information needs[53] relevant to environmental fate								
1205485	3407162	4422636	4674228	4683774	4683981	4684004	4684038	4684048
1612136	4275027	4428186	4674230	4683778	4683982	4684005	4684039	4684049
1614234	4399677	4429336	4674231	4683782	4683983	4684006	4684040	4684061
1962870	4409714	4432999	4674232	4683785	4683984	4684008	4684042	4684065
2044953	4410096	4670341	4674235	4683975	4683985	4684011	4684043	4684067
2046206	4415908	4674220	4674238	4683976	4683986	4684012	4684044	4684079
2960791	4419365	4674222	4674239	4683977	4683987	4684016	4684045	4684080
3037506	4421781	4674224	4674889	4683979	4683988	4684019	4684046	4684083
3039332	4421783	4674225	4683772	4683980	4683993	4684021	4684047	4684086
Reference excluded (HERO ID) because the reference did NOT present quantitative environmental fate data								
N/A.								

[53] 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.12: 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	3038919 4731312 4731313
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	N/A.
Is this primarily a modeling/simulation study? [Note: Select "Yes" only if there is no experimental verification]	Yes	N/A.

Table C.13: 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). **OR** The vehicle used in the study was likely to unduly influence the study results.	N/A.
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**	N/A.

Table C.13: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Fate		
Data quality metric	**Unacceptable if:**	**References excluded (HERO ID)**
	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.	
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).	N/A.
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.	N/A.
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**	N/A.

Table C.13: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Fate		
Data quality metric	**Unacceptable if:**	**References excluded (HERO ID)**
	Data indicate that disappearance or transformation of the parent compound was likely due to some other process.	
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).	N/A.