Supporting Information for Low-Priority Substance 2-Propanol, 1,1'-oxybis- (CASRN 110-98-5) (1,1'-Dimethyldiethylene Glycol)

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 substances 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. 2-Propanol, 1,1'-oxybis-, referenced as 1,1'-dimethyldiethylene glycol for the remainder of this document, is one of the 40 chemical substances initiated for prioritization as referenced in a March 21, 2019 notice (84 FR 10491)[1] and one of the 20 proposed as low-priority substances in an August 15, 2019 notice (84 FR 41712).[2]

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

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

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

The screening review is not a risk evaluation, but rather a review of reasonably available information on the chemical substance that relates to the specific criteria and considerations in TSCA section 6(b)(1)(A)

[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).

and 40 CFR 702.9. This paper documents the results of the screening review which supports the final designation of 1,1'-dimethyldiethylene glycol 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.

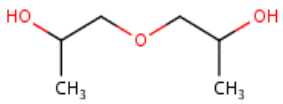
- *Appendix A (Conditions of Use Characterization):* This appendix contains a comprehensive list of TSCA and non-TSCA uses for the chemical substance from publicly available databases.

- *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 1,1-Dimethyldiethylene Glycol

Table 1 below provides the CAS number, synonyms, and other information on 1,1'-dimethyldiethylene glycol.

Table 1: 1,1-Dimethyldiethylene Glycol at a Glance	
Chemical Name	1,1'-Dimethyldiethylene Glycol
CASRN	110-98-5
Synonyms	1,1'-oxydi-2-propanol; 1,1'-Oxydipropan-2-ol; 2-Propanol, 1,1'-oxybis-; 1,1'-Oxybis-2-propanol; 2,2'-Dihydroxydipropyl ether; 2-Propanol, 1,1'-oxydi-
Trade Name(s)	NIAX Catalyst D-19
Molecular Formula	$C_6H_{14}O_3$
Representative Structure	
Source(s): Kim et al. (2016); NLM (2018a)	

1,1'-Dimethyldiethylene glycol is a branched isomer of bis(hydroxypropyl) ether. 1,1'-Dimethyldiethylene glycol is produced as a byproduct or coproduct of the manufacture of propylene glycol. 1,1'-Dimethyldiethylene glycol is a colorless, nearly odorless, and slightly viscous liquid with a high boiling point. It is completely soluble in water and can also dissolve oils. In addition, 1,1'-dimethyldiethylene glycol is hygroscopic and acts as a humectant, which means it absorbs water and increases hydration in products. 1,1'-Dimethyldiethylene glycol also functions as a plasticizer and as a plasticizer intermediate in the formation of polyurethane polyols to give improved flexibility and resistance to cracking at low temperatures. A plasticizer is a substance that is added to a material to alter its physical properties, mainly to increase flexibility or decrease viscosity. These properties make 1,1'-dimethyldiethylene glycol a multifunctional ingredient used in a variety of applications and product sectors. Section 5 includes conditions of use for this chemical.

3. Physical-Chemical Properties

Table 2 lists physical-chemical properties for 1,1'-dimethyldiethylene glycol. 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 1,1'-Dimethyldiethylene Glycol

Source/ Model	Data Type	Endpoint	Endpoint value	Notes
HSDB 2019	Experimental	Physical state at room temp (based on melting point)	Liquid (< -40°C)	
HSDB 2019; International Chemical Safety Card, 2017; OECD SIDS, 2001; Chadwick 1988	Experimental	Molecular weight	134 g/mol	
EPISuite v.4.11[4]	Calculated	Molecular weight	134.18 g/mol	
Lyman 1990	Experimental	Molar volume	166 cm^3/mol	
HSDB	Experimental	Water solubility	$1.00x10^5$ mg/L	The PhysProp database reports a measured water solubility of 0.1 mg/L. This appears to be in error, (1) because it is too low and (2) HSDB reports a value of 100 g/L citing the same source (CITI, Japan).
International Chemical Safety Card; OECD SIDS 2001	Experimental	Water solubility	1000000 mg/L (miscible)	
EPISuite v.4.11	Estimated	Water solubility	$1.0x10^6$ mg/L	
International Chemical Safety Card; OECD SIDS 2001	Experimental	Water solubility	7.45 mol/L	
HSDB	Experimental	Water solubility	$7.45x10^{-1}$ mol/L	
Reported to the ECHA database	Experimental	Log K_{ow}	-0.462 at 21.7°C and pH 6	

[4] EPI Suite Physical Property Inputs – Boiling Point = 232.8 deg C, Melting Point = -40 deg C, Vapor Pressure = 0.03 mm Hg, Water Solubility = 1000000 mg/L, Log P = -0.7, SMILES: OC(C)COCC(C)O

Table 2: Physical-Chemical Properties for 1,1'-Dimethyldiethylene Glycol				
Source/ Model	**Data Type**	**Endpoint**	**Endpoint value**	**Notes**
International Chemical Safety Card 2019	Experimental	Log K_{ow}	-0.7/-1.5	
OECD SIDS 2001	Experimental	Log K_{ow}	-1.486; -0.687	
EPISuite v.4.11	Estimated	Log K_{ow}	-0.64	
EPISuite v.4.11	Estimated	Log K_{oa}	6.14	
EPISuite v.4.11	Estimated	Log K_{oc}	0 (MCI); -0.38 (K_{ow})	
HSDB; International Chemical Safety Card 2019	Experimental	Vapor pressure	0.03 mm HG (4 Pa) at 25°C	
OECD SIDS 2001	Experimental	Vapor pressure	< 0.075 at 20 °C; < 0.01 at 20 °C; 0.04 at 21 °C	
Chadwick 1988	Experimental	Vapor pressure	<0.0075 (0.001 kPa) at 20 °C	
EPISuite v.4.11	Estimated	Vapor pressure	$6.28x10^{-3}$ mm HG	
EPISuite v.4.11	Estimated	Henry's Law	<1E-8 atm-m^3/mole	
EPISuite v.4.11	Estimated	Volatilization	5300 days (river) 58000 days (lake)	
EPISuite v.4.11	Estimated	Photolysis (Indirect)	4.1 hours ($T_{1/2}$)	• OH rate constant 3.31 E-11 cm^3/molecules-second (12 hour day; 1.5E6 OH/cm^3) • No ozone prediction
EPISuite v.4.11	Estimated	Hydrolysis	Rate constants cannot be estimated	No reactive functional groups
EPISuite v.4.11	Estimated	Biodegradation potential	Ready prediction: Yes	
EPISuite v.4.11	Estimated	Wastewater treatment plant removal	80.7% Total Removal (80.2% biodegradation, 0.5% sludge, 0% air)	Reference: HSDB, 110-98-5 http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB
EPISuite v.4.11	Estimated	BAF	0.9	
EPISuite v.4.11	Estimated	BCF	3.16	Based on regression equation

Based on its reported physical form and melting point, 1,1'-dimethyldiethylene glycol is a liquid under ambient conditions (HSDB 2019). Exposure through direct dermal contact with the substance is possible, but concern is lessened because this chemical is a slow skin penetrant (discussed in Section 6.1.1) and likely to be minimally absorbed through skin based on its molecular weight, water solubility and log K_{ow}. Because of its measured vapor pressure (OECD SIDS, 2001), 1,1'-dimethyldiethylene glycol is expected to be volatile when in neat form at ambient temperatures. As a result, exposure to 1,1'-dimethyldiethylene glycol is possible through inhalation of vapors or aerosols if they are generated. Based on measured solubility data (HSDB, 2019), 1,1'-dimethyldiethylene glycol is considered water soluble, indicating the potential for this substance to dissolve in water and form an aqueous solution. 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 if 1,1'-dimethyldiethylene glycol is present in diluted form. The estimated Henry's Law constant (EPI Suite, 2019) for 1,1'-dimethyldiethylene glycol indicates volatilization from water and aqueous solutions is not expected; therefore, exposure through breathing vapor from a dilute form is expected to be minimal. Absorption and sequestration in fatty tissues are unlikely, as reflected in the estimated bioconcentration (BCF) and bioaccumulation (BAF) values for this compound (EPI Suite, 2019). The estimated log K_{oc} (EPI Suite, 2019) indicates this substance is highly mobile in soils, increasing its potential for leaching into groundwater, including ground water sources of drinking water. If oral exposure occurs via ingestion of contaminated drinking water, including well water, absorption through the gastrointestinal tract is likely based on experimental evidence (discussed in Section 6.1.1). Concern for presence in drinking water is reduced in part by 1,1'-dimethyldiethylene glycol's expected low persistence based on read-across from closely-related analogs (discussed in Section 6.3.1) and low-hazard findings from toxicological studies of organisms exposed to a closely-related analog in drinking water (discussed in Section 6.1).

3.1 References

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Hazardous Substance Database (HSDB). (2016). 2,2'-Dihydroxydi-n-propyl ether. Retrieved from https://toxnet.nlm.nih.gov/

European Chemicals Agency (ECHA). (2019). 1,1'-oxydipropan-2-ol. Retrieved from https://echa.europa.eu/substance-information/-/substanceinfo/100.003.475

International Chemical Safety Card (ICSC). (2019). Retrieved from https://www.ilo.org/dyn/icsc/showcard.display?p_lang=en&p_card_id=1055&p_version=2

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

OECD SIDS (2001). Dipropylene glycol (mixed isomers and dominant isomer Cas No: 25265-71-8 and 110-98-5 https://heronet.epa.gov/heronet/index.cfm/reference/download/reference_id/4940388

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

4. Relevant Assessment History

EPA assessed the toxicological profile of 1,1'-dimethyldiethylene glycol and added the chemical to the Safer Choice Program's Safer Chemical Ingredients List (SCIL) in December 2012 under the functional class of solvents. The SCIL[5] is a continuously updated list of chemicals that meet low-concern Safer Choice criteria.[6]

EPA also reviewed international assessments of 1,1'-dimethyldiethylene glycol. EPA identified assessments by the Organisation for Economic Co-operation and Development (OECD), and government agencies in Canada, Germany, and Japan.

The Organisation for Economic Co-operation and Development (OECD) Screening Information Datasets (SIDS) Initial Assessment Meeting (SIAM) discussed the SIDS Initial Assessment Report (SIAR) on 1,1'-dimethyldiethylene glycol (dipropylene glycol, mixed isomers and dominant isomer), in January 2001. The SIAM determined this chemical to be "low priority for further work" for human health and the environment.[7]

The Canadian Government, through an assessment of toxicity and exposure as part of its categorization of the Domestic Substance List, found that 1,1'-dimethyldiethylene glycol did not meet its criteria for further attention.[8]

Japan's National Institute of Technology and Evaluation (NITE) categorized 1,1'-dimethyldiethylene glycol as Exposure Class 4 in 2017, which is the lowest concern hazard ranking assigned.[9]

The German Environment Agency (UBA) designated 1,1'-dimethyldiethylene glycol as "low hazard to waters" in August 2017 based on an assessment of ecotoxicity and environmental fate.[10]

[5] https://www.epa.gov/saferchoice/safer-ingredients
[6] https://www.epa.gov/sites/production/files/2013-12/documents/dfe_master_criteria_safer_ingredients_v2_1.pdf
[7] https://hpvchemicals.oecd.org/ui/handler.axd?id=40da06b1-a855-4c0c-bc21-bbc856dca725
[8] https://canadachemicals.oecd.org/ChemicalDetails.aspx?ChemicalID=AD9A3337-870A-4CE5-8E04-DACE72B5D465
[9] http://www.safe.nite.go.jp/jcheck//direct.action?TYPE=DPAGE1&CAS=110-98-5&MITI=2-413
[10] https://webrigoletto.uba.de/rigoletto/public/searchDetail.do?kennummer=2618

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 1,1'-dimethyldiethylene glycol (Appendix A) to inform which uses would be determined conditions of use.[11] 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).

According to CDR, 1,1'-dimethyldiethylene glycol is manufactured domestically and imported. It is used in processing (incorporation into formulation, mixture or reaction) for plastics product manufacturing, soap, cleaning compound, and toilet preparation manufacturing; it is also used in processing plastic material and resin. Examples of industrial uses include construction and building materials and mining support activities. Consumer and commercial uses include air care products; cleaning and furnishing care products; laundry and dishwashing products; plastic and rubber products; arts and crafts; and toys, among others. Based on the known manufacturing, processing, and uses of this chemical substance, EPA assumes distribution in commerce. In the 2016 CDR, two facilities reported that 1,1'-dimethyldiethylene glycol was not recycled (which could mean recycled, reprocessed, or reused). For one facility, recycling information was withheld. No information on disposal is found in CDR or through EPA's Toxics Release Inventory (TRI) Program[12] because 1,1'-dimethyldiethylene glycol is not a TRI-reportable chemical. Although reasonably available information did not specify additional types of disposal, for purposes of this prioritization designation, EPA assumed end-of-life pathways that include releases to air, wastewater, surface water, and land via solid and liquid waste based on the conditions of use (e.g., incineration, landfill).

To supplement CDR, EPA conducted research through the publicly available databases listed in Appendix A (Table A.2) and performed additional internet searches to clarify conditions of use or find additional occupational[13] and consumer uses. This research improved the Agency's understanding of the conditions of use for 1,1'-dimethyldiethylene glycol. Although EPA identified uses of 1,1'-dimethyldiethylene glycol 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 1,1'-dimethyldiethylene glycol 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).

[11] 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).

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

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

Table 3: Conditions of Use for 1,1'-Dimethyldiethylene Glycol			
Life Cycle Stage	**Category**	**Subcategory of Use**	**Source**
Manufacturing	Import	Import	EPA (2017b)
Processing	Processing- incorporation into formulation, mixture or reaction	Plasticizers – plastics product manufacturing	EPA (2017b)
		Odor agents - soap, cleaning compound, and toilet preparation manufacturing; all other chemical product and preparation manufacturing	
	Processing—incorporation into article	Odor agents - plastic material and resin manufacturing	
	Industrial manufacturing	Automotive care, automotive fuel, automotive manufacturing; detergents manufacturing; electronic equipment manufacturing; furniture manufacturing; leather manufacturing; machinery and equipment manufacturing; paints, varnishes, and coatings manufacturing; paper, pulp, and paper product manufacturing; perfumes manufacturing; textile manufacturing; transport equipment manufacturing	CPCat (2019); Synapse Information Resources (2009)
	Fabricated metal product manufacturing	Fabricated metal products; metal treatment and coating	
	Construction and building materials covering large surface areas	Wood manufacturing	CPCat (2019)
		Food-contact metallic manufacturing	Synapse Information Resources (2009)
	Recycling	Recycling	EPA (2017b)[14]
Distribution	Distribution	Distribution	EPA (2017b)
Industrial	Construction and building materials covering large surface areas	Boat and ship building; construction; floor and wall materials; glass building materials	CPCat (2019); Synapse Information Resources (2009)
	Mining (except oil and gas) support activities	Mining (except oil and gas) support activities	
	Other	Industrial cleaning	
Industrial/ commercial		Anti-foaming agents	CPCat (2019)
Commercial		Ostomy bag deodorizer	Medline.com (2017)
Commercial/	Air care products		

[14] In the 2016 CDR, two facilities reported that 1,1'-dimethyldiethylene glycol was not recycled (which could mean recycled, reprocessed, or reused). For one facility, recycling information was withheld. No further information about recycling or disposal was found.

Table 3: Conditions of Use for 1,1'-Dimethyldiethylene Glycol			
Life Cycle Stage	**Category**	**Subcategory of Use**	**Source**
consumer	Cleaning and furnishing care products		EPA (2017b); CPCat (2019)
	Laundry and dishwashing products		
	Plastic and rubber products not covered elsewhere		
Consumer	Arts, crafts, and hobby materials;	Marker pens	CPCat (2019)
	Furniture and furnishings not covered elsewhere	Baby mattresses and pillows	
	Décor candle		
	Printing inks		
Unknown		Hydraulic brake fluid; windshield washing agents; degreasers; lime deposit (calcium) remover; textile detergent; food and beverage service activities; food-contact coatings; food packaging; fuel additive; petroleum additive; absorbents/adsorbents; adhesives and binding agents; colorant; corrosion inhibitor; polishing agent; preservatives	Synapse Information Resources (2009); CPCat (2019)
Disposal	Releases to air, wastewater, solid and liquid wastes		Though not explicitly identified, releases from disposal were assumed to be reasonably foreseen[15]

[15] 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 primary literature and other data sources to identify reasonably available information on hazard for 1,1'-dimethyldiethylene glycol. This literature review approach[16] 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 1,1'-dimethyldiethylene glycol against the endpoints listed below. EPA's New Chemicals Program has used these endpoints for decades to evaluate chemical substances under TSCA[17] 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[18] 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.

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[19]	**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

[16] 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.

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

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

[19] 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)[20]		**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[21]		**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[22]	**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		

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

[21] 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).

[22] 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[23]	**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[24] evidence in humans)	Negative studies or robust mechanism-based SAR
Sensitization[25]		**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[26]	**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

[23] 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).

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

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

[26] 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)[27]	**Chronic Aquatic Toxicity Value (L/E/IC50)[27]**	**Persistence (Measured in terms of level of biodegradation)[28]**	**Bioaccumulation Potential[29]**
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

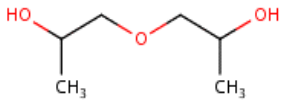
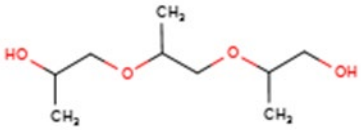
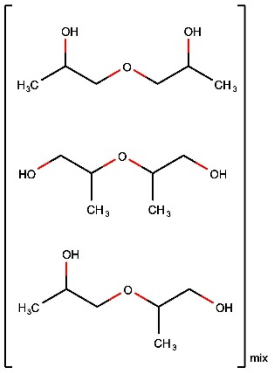
Below is a summary of the reasonably available information that EPA included in the hazard evaluation of 1,1'-dimethyldiethylene glycol. In many cases, EPA used analogous chemicals to make findings for a given endpoint. Where this is the case, use of the analog is explained. If the chemical studied is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

1,1'-Dimethyldiethylene glycol is a branched isomer of bis(hydroxypropyl) ether generated as a byproduct or coproduct in the manufacture of propylene glycol when some of the propylene glycol formed reacts with unreacted propylene oxide (methyl oxirane) feedstock. The methyl groups are specified to be at the 1 and 1' positions. EPA used best professional judgement to select analogs for 1,1'-dimethyldiethylene glycol based on similarity in structure, physical-chemical properties, and functionality, with the assumption that these chemicals will have similar environmental transport and persistence characteristics, and bioavailability and toxicity profiles. Both of the analogs listed in Table 5 are oligomeric propylene glycols like the 1,1'-dimethyldiethylene glycol. The analog dipropylene glycol is a mixture of three branched isomers of bis(hydroxypropyl) ether, formed by addition of unreacted propylene oxide to propylene glycol, and differing only in the placement of the methyl substituents. 1,1'-Dimethyldiethylene glycol is one of the components of dipropylene glycol. The analog tripropylene glycol is a mixture of branched isomers generated as byproducts or coproducts in the manufacture of propylene glycol when some of the dipropylene glycol formed reacts with unreacted propylene oxide feedstock. The positions of the methyl groups in the product are unspecified. Differences in the methyl group positions in these chemicals are not expected to significantly affect their chemical and hazard profiles. Based on these factors, the environmental and toxicological effects of tripropylene glycol and dipropylene glycol are expected to be very similar to each other and to 1,1'-dimethyldiethylene glycol.

[27] 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).*

[28] 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)*.

[29] 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: 1,1'-Dimethyldiethylene Glycol and Analog Structures		
CASRN	**Name**	**Structure**
110-98-5	**1,1'-Dimethyldiethylene glycol**	 Representative structure
24800-44-0	**Tripropylene glycol (mixed isomers)**	 Representative structure
25265-71-8	**Dipropylene glycol (mixed isomers)**	 Representative structure

6.1.1 Absorption, Distribution, Metabolism, and Excretion

Absorption

To assess 1,1'-dimethyldiethylene glycol's absorption potential from the gastrointestinal tract, EPA used experimental studies from analogs. In a study on dogs, dipropylene glycol was rapidly absorbed from the gastrointestinal tract and was no longer detectable in the blood 24 hours after an oral exposure (BUA, 1996). Rats exposed to ^{14}C-tripropylene glycol by oral gavage also rapidly absorbed tripropylene glycol, as indicated by recovery of 91.4% of the administered dose 24 hours following exposure (Reported to the ECHA database, 1995a). Based on these data, 1,1'-dimethyldiethylene glycol is expected to be absorbed after oral exposures.

In vitro studies were used to assess the potential dermal absorption by 1,1'-dimethyldiethylene glycol using read-across from dipropylene glycol. Excised abdominal skin from human cadavers demonstrated dipropylene glycol is a slow penetrant, with the results demonstrating a permeability

coefficient of 3.85 x 10^{-5} cm/hour (Fasano et al., 2011; Reported to the ECHA database, 2007b; Fasano, 2007). Based on these data, potential for absorption of 1,1'-dimethyldiethylene glycol through the skin is low.

Based on its low molecular weight and high water solubility (discussed in Section 3), 1,1'-dimethyldiethylene glycol is expected to be absorbed from the lungs if inhaled.

Distribution

1,1'-Dimethyldiethylene glycol is considered water soluble based on its physical-chemical properties (Table 2) and is likely to be distributed mainly in aqueous compartments in an organism. This prediction is supported by experimental evidence on the analog tripropylene glycol. Rats exposed to tripropylene glycol by oral gavage displayed radiolabeled tripropylene glycol in the tissues and the carcass 24 hours following exposure (OECD, 2001; Reported to the ECHA database, 1995a). Specifically, tripropylene glycol was reported in the liver at 0.20%, kidneys at 0.09%, carcass at 0.06%, blood at 0.03%, and skin, brain, muscle, and fat at less than 0.03% (as percent of the administered dose per gram of tissue). These data indicate tissue distribution of tripropylene glycol to the liver and kidney and provide evidence that 1,1'-dimethyldiethylene glycol will be rapidly distributed following oral absorption.

Metabolism

To assess 1,1'-dimethyldiethylene glycol's metabolism pathways, EPA used experimental studies from analogs. Oral administration of tripropylene glycol to rats resulted in rapid metabolism to dipropylene glycol, then to propylene glycol, which is converted to lactic and pyruvic acids or excreted in the urine. Lactate and pyruvate may be further metabolized through the citric acid cycle to yield carbon dioxide and water or may be stored as glycogen (OECD, 2001). Rats exposed to ^{14}C-tripropylene glycol by oral gavage excreted approximately 13% as free or conjugated tripropylene glycol, approximately 8.4% as free and conjugated dipropylene glycol, and approximately 3.9% as free and conjugated propylene glycol (OECD, 2001; Reported to the ECHA database, 1995a). These data on closely-related analogs indicate that 1,1'-dimethyldiethylene glycol will be rapidly metabolized.

Excretion

To assess 1,1'-dimethyldiethylene glycol's excretion pathways, EPA used experimental evidence from tripropylene glycol. Following the oral administration of tripropylene glycol to rats, 52% was recovered in urine, 21% in exhaled CO_2, and 5% in the feces after 24 hours (Reported to the ECHA database, 1995a). These data suggest that 1,1'-dimethyldiethylene glycol will be excreted from the body, as opposed to accumulating in tissues, following exposure.

6.1.2 Acute Toxicity

EPA assessed the potential for mammalian toxicity from acute exposure by 1,1'-dimethyldiethylene glycol using results from oral, inhalation, and dermal studies.

Two studies on rats exposed to 1,1'-dimethyldiethylene glycol by oral gavage reported LD_{50}s at very high doses, such as 12500 mg/kg and 16195 mg/kg respectively (Dow Chemical, 1994; Union Carbide, 1994). Another study in guinea pigs exposed to 1,1'-dimethyldiethylene glycol by oral gavage reported an LD_{50} of 10000 mg/kg (Union Carbide, 1994). These results provide sufficient

information to indicate low concern for acute toxicity with LD_{50}s above the low-concern benchmark of 2000 mg/kg for oral exposures.

A study on rabbits exposed to dipropylene glycol dermally reported no adverse effects at the single dose tested (5010 mg/kg), resulting in an LD_{50} greater than 5010 mg/kg (Reported to the ECHA database, 1995c). Another study on rabbits exposed to tripropylene glycol dermally reported no adverse effects at the single dose tested, resulting in an LD_{50} greater than 16320 mg/kg (Reported to the ECHA database, 1974a). These results provide sufficient information to indicate low concern for acute toxicity with LD_{50}s above the low-concern benchmark of 2000 mg/kg for dermal exposures.

A study on rats exposed to a single concentration of tripropylene glycol in saturated vapor for eight hours and then observed for two weeks reported no mortalities (Reported to the ECHA database, 1974b). Based on tripropylene glycol's vapor pressure of 0.00195 torr, the expected air saturation concentration for tripropylene glycol is around 0.02 mg/L at room temperature, which is below the study concentration of 0.083 mg/L, indicating no adverse effects are expected at the complete air saturation concentration. Another study on rats exposed to a dipropylene glycol aerosol reported no adverse effects at the single dose tested, resulting in an LC_{50} greater than 2.34 mg/L (Reported to the ECHA database, 1995d). Considering the chemical's physical chemical properties (see Section 3) and available experimental data, these results provide sufficient information to indicate 1,1'-dimethyldiethylene glycol is of low concern for acute toxicity from inhalation exposures based on no adverse effects reported at expected air saturation.

6.1.3 Repeated Dose Toxicity

EPA assessed the potential for mammalian toxicity from repeated exposures by 1,1'-dimethyldiethylene glycol using read-across from tripropylene glycol. In a combined repeated dose, reproductive, and developmental study (OECD, 1994; Reported to the ECHA database, 1993b), rats were exposed to tripropylene glycol via oral gavage for 49 days, beginning 14 days prior to mating and through lactation day 3 for females. The no observed adverse effect level (NOAEL) was 200 mg/kg-day and the lowest observed adverse effect level (LOAEL) was 1000 mg/kg-day based on changes in organ weight in parents.

EPA also assessed the potential for toxicity from repeated exposures to dipropylene glycol in drinking water. A study on mice exposed to dipropylene glycol in drinking water for 13 weeks demonstrated a NOAEL of 2620 mg/kg-day and a LOAEL of 4790 mg/kg-day based on increased liver weight (Reported to the ECHA database, 2004g; NTP, 2004). A study on rats exposed to dipropylene glycol in drinking water for 14 weeks demonstrated a NOAEL of 425 mg/kg-day and a LOAEL of 890 mg/kg-day based on relative liver weight (Reported to the ECHA database, 2004f; NTP, 2004). A 2-year study on mice exposed to dipropylene glycol in drinking water demonstrated a NOAEL of 1040 mg/kg-day and a LOAEL of 1950 mg/kg-day based on decreased mean body weight (Reported to the ECHA database, 2004e; NTP, 2004). Another study on rats exposed to dipropylene glycol for 2 years in drinking water demonstrated a NOAEL of 115 mg/kg-day and a LOAEL of 470 mg/kg-day based on incidence of nephropathy, focal histiocytic and focal granulomatous inflammation in male livers (Reported to the ECHA database, 2004b, d; NTP, 2004).

All of these analog results provide sufficient information to indicate low concern for toxicity resulting from repeated exposures by exceeding the oral low-concern benchmark of 100 mg/kg-day for a 90-day study.

6.1.4 Reproductive and Developmental Toxicity

EPA assessed the potential for reproductive toxicity using read-across from analog tripropylene glycol. In a combined repeated dose, reproductive, and developmental study, rats were exposed to tripropylene glycol via oral gavage for 49 days, beginning 14 days prior to mating and continuing through lactation day 3 for females. The authors reported no reproductive (mating, fertility, and estrus cycle) or developmental effects (external examinations of the pups and pup body weight gain) at the highest dose tested (1000 mg/kg-day). EPA determined the NOAEL for this study was 1000 mg/kg-day (OECD, 1994). These analog results provide sufficient information to indicate low concern for reproductive toxicity in the target chemical by exceeding the 250 mg/kg-day benchmark.

EPA further assessed the potential for developmental toxicity, using read-across from an analog, dipropylene glycol. A study on pregnant rats orally exposed to dipropylene glycol during GD 6-15 reported a developmental NOAEL of 2000 mg/kg-day and a LOAEL of 5000 mg/kg-day based on decreased fetal weight. A study on rabbits orally exposed to dipropylene glycol during GD 6-19 reported no adverse effects at the highest dose tested, resulting in a NOAEL of 1200 mg/kg-day (OECD, 2001; Bates et al., 1992a; Reported to the ECHA database, 1990a). These analog results provide sufficient information to indicate low concern for developmental toxicity by exceeding the 250 mg/kg-day benchmark.

6.1.5 Genotoxicity

EPA assessed experimental studies on genotoxicity as a potential indicator of genotoxic carcinogenicity using read-across from dipropylene glycol. Three *in vitro* gene mutation studies resulted in negative findings from dipropylene glycol exposure with and without metabolic activation in *Salmonella typhimurium* (Reported to the ECHA database, 2004c; NTP, 2004; Reported to the ECHA database, 1992a) and in mouse lymphoma cells (Reported to the ECHA database, 1988). Further, a mouse *in vivo* study indicated negative results for chromosomal aberrations in the form of micronucleated polychromatic erythrocytes from dipropylene glycol exposure (OECD, 2001; Reported to the ECHA database, 1999). These negative results in an analog provide sufficient information to indicate 1,1'-dimethyldiethylene glycol has low concern for inducing genotoxicity.

6.1.6 Carcinogenicity

EPA assessed the potential for 1,1'-dimethyldiethylene glycol to cause carcinogenicity in mice and rats using read-across from dipropylene glycol. Rats exposed to dipropylene glycol in drinking water for 2 years demonstrated no dose-related effects on cancer incidence or cancer-related effects at the highest dose tested (3040 mg/kg-day in males, 2330 mg/kg-day in females), resulting in a negative finding for carcinogenicity (Reported to the ECHA database, 2004b; NTP, 2004). Similarly, mice exposed to dipropylene glycol in drinking water for two years also demonstrated no adverse effects at the highest dose tested (2390 mg/kg-day in males, 1950 mg/kg-day in females), resulting in a negative finding for carcinogenicity (Reported to the ECHA database, 2004a; NTP, 2004). Using read-across from this analog, these negative results provide sufficient information to indicate low concern for carcinogenicity for 1,1'-dimethyldiethylene glycol.

6.1.7 Neurotoxicity

While no traditional neurotoxicity studies were available for 1,1'-dimethyldiethylene glycol or closely-related analogs, EPA assessed the potential for neurotoxicity using relevant endpoints measured in acute and repeated dose studies and using accepted new approach methodologies (NAMs), such as U.S. EPA's ToxCast.[30]

Several repeat dose oral studies in rats and mice for analog tripropylene glycol reported no effects on the limited neurological endpoints that were evaluated (i.e., brain histopathology only). Tripropylene glycol did not produce histopathological lesions in the brain of rats at doses up to 1000 mg/kg-day (highest dose tested) in a study when males were exposed for 49 days and females were exposed from 14 days prior to mating until day 3 of lactation (OECD, 1994; Reported to the ECHA database, 1993b). Dipropylene glycol did not produce histopathological brain lesions in rats at oral doses up to 12,800 mg/kg-day for 3 months or up to 3040 mg/kg-day for 2 years. Similarly, in mice, no brain lesions were observed at oral doses up to 14700 mg/kg-day for 3 months or up to 2330 mg/kg-day for 2 years (Reported to the ECHA database, 2004b, d; NTP, 2004). A study on rats acutely exposed to dipropylene glycol by oral gavage noted decreased motor activity and ataxia for a few hours after exposure to the high dose of 5010 mg/kg, but the effects subsided by the first day of the observation period (Reported to the ECHA database, 1995e).

ToxCast results for 1,1'-dimethyldiethylene glycol included 15 *in vitro* high throughput biochemical- and cell-based assays related to neurological functions.[31] Bioactivity was not induced in any assay by 1,1'-dimethyldiethylene glycol.

These data provide sufficient information to indicate there is low concern for neurotoxicity associated with 1,1'-dimethyldiethylene glycol. This finding is also supported by the low-hazard findings for other human health hazard endpoints, including toxicity from acute exposures, reproductive toxicity, and developmental toxicity.

6.1.8 Skin Sensitization

EPA assessed the potential for 1,1'-dimethyldiethylene glycol to cause skin sensitization using available experimental studies in an analog, dipropylene glycol. Dipropylene glycol demonstrated negative results in guinea pigs (Reported to the ECHA database, 1995k) and in two human studies (Reported to the ECHA database, 1995h; Johansen et al., 1995; Leberco Labs, 1994). These negative analog results provide sufficient information to indicate low concern for skin sensitization for 1,1'-dimethyldiethylene glycol.

[30] https://comptox.epa.gov/dashboard Chemical specific assay list can be found at https://comptox.epa.gov/dashboard/dsstoxdb/results?search=DTXSID7026863

[31] EPA reviewed reasonably available information in the ToxCast database for neurological functions. Reference: Chushak Y., Shows H., Gearhart J., Pangburn H. 2018. In silico identification of protein targets for chemical neurotoxins using Toxcast in vitro data and read-across within the QSAR toolbox. Toxicology Research issue 3. Supplemental files: https://pubs.rsc.org/en/content/articlelanding/2018/tx/c7tx00268h#!divAbstract.

6.1.9 Respiratory Sensitization

Experimental data determined to be of adequate quality[32] on 1,1'-dimethyldiethylene glycol or closely related analogs were not reasonably available for the assessment of respiratory sensitization potential for 1,1'-dimethyldiethylene glycol, EPA used NAMs, such as the QSAR Toolbox, version 4.2 models[33] 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 1,1'-dimethyldiethylene glycol. 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[34] on 1,1'-dimethyldiethylene glycol 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 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 1,1'-dimethyldiethylene glycol, 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 1,1'-dimethyldiethylene glycol.

6.1.11 Skin Irritation

EPA assessed the potential for dermal irritation using read-across from dipropylene glycol and tripropylene glycol. Three studies in rabbits demonstrated negative results for dermal irritation by dipropylene glycol (Reported to the ECHA database, 1995c, j; Leberco Labs, 1994). One study in

[32] 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.

[33] 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

[34] 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.

rabbits demonstrated tripropylene glycol was minimally irritating with mean irritation score of 2 out of 10 (Reported to the ECHA database, 1974d). In another study, humans exposed to dipropylene glycol demonstrated mild erythema in 4 of the 33 subjects at the 24 hour scoring (Reported to the ECHA database, 1995f). However, humans exposed to tripropylene glycol for 24 hours reported negative results for skin irritation (Reported to the ECHA database, 1995b). A longer dermal patch study on humans exposed to tripropylene glycol for 14 days also indicated negative results for skin irritation (Reported to the ECHA database, 1997). These results on analogs provide sufficient information to indicate 1,1'-dimethyldiethylene glycol is expected to be of low concern for skin irritation.

6.1.12 Eye Irritation

To assess potential for eye irritation, EPA used read-across from two analogs, dipropylene glycol and tripropylene glycol. Rabbits exposed to tripropylene glycol displayed mild conjunctival redness, chemosis, and conjunctival discharge at the 1-hour scoring, but these results were fully reversible by 24 hours, leading to a negative result for eye irritation (Reported to the ECHA database, 2010a). Similarly, rabbits exposed to dipropylene glycol displayed conjunctival redness and a subset displayed chemosis after one hour, but these results were also fully reversible by 24 hours, leading to a negative result for eye irritation (Reported to the ECHA database, 1995g). These results are supported by two studies with negative results in rabbits exposed to dipropylene glycol (Leberco Labs, 1994) and tripropylene glycol (Reported to the ECHA database, 1974c). Additionally, an *in vitro* human corneal epithelium model study (Reported to the ECHA database, 2010b) also reported tripropylene glycol as negative for inducing ocular irritation. These *in vivo* and *in vitro* results in analogs provide sufficient information to indicate low concern for eye irritation by 1,1'-dimethyldiethylene glycol.

6.1.13 Hazards to Potentially Exposed or Susceptible Subpopulations

The above information supports a low human health hazard finding for 1,1'-dimethyldiethylene glycol 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 1,1'-dimethyldiethylene glycol.

6.2 Environmental Hazard

To review environmental hazard endpoints without adequate quality[32] 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 1,1'-dimethyldiethylene glycol based on estimated toxicity values using the Ecological Structure Active (ECOSAR) Predictive Model[35] and available experimental data from two analogs, dipropylene glycol and tripropylene glycol. Appendix B contains a summary of the reasonably available environmental hazard data.

[35] 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 using read-across from tripropylene glycol and dipropylene glycol. No adverse effects were observed in aquatic invertebrates exposed to dipropylene glycol (Reported to the ECHA database, 2002, 1995i) or tripropylene glycol (Reported to the ECHA database, 2010c, 1994a; OECD, 1994) at the highest doses tested (100 mg/L and 1000 mg/L, respectively), resulting in LC_{50}s greater than 100 mg/L and 1000 mg/L, respectively, for invertebrates. Similarly, no effects were observed in aquatic vertebrate or algae exposed to tripropylene glycol resulting in LC_{50}s greater than 1000 mg/L for aquatic vertebrates (Reported to the ECHA database, 1994b; OECD, 1994) and algae (OECD, 1994). These aquatic toxicity studies provide sufficient information to indicate low concern for acute aquatic exposure by exceeding the low-concern benchmark of 100 mg/L.

6.2.2 Chronic Aquatic Toxicity

Chronic toxicity values estimated by ECOSAR for aquatic vertebrates, aquatic invertebrates, and algae were 1300 mg/L, 420 mg/L, and 370 mg/L, respectively. These toxicity values provide sufficient information to indicate that 1,1'-dimethyldiethylene glycol is expected to have low environmental hazard based on the low-concern criteria chronic aquatic toxicity benchmark of 10 mg/L.

6.3 Persistence and Bioaccumulation Potential

6.3.1 Persistence

Varied results are observed in the experimental ready test data presented in Appendix B. Due to the differences in the test conditions of the OECD ready test methods, some of this variability is likely a result of performance under different test designs rather than an inherent limitation of the biodegradability of the test substance. Given the varied results, EPA relied on studies from analogs tripropylene glycol and dipropylene glycol to make a weight of the scientific evidence conclusion. An explanation of ready and inherent biodegradation tests is provided below.

Ready biodegradation tests are stringent test methods in which a high concentration of test substance is evaluated using a non-adapted inoculum. Passing this type of test indicates that a chemical is likely to biodegrade rapidly in the environment and has low potential for persistence. However, not passing the ready criteria is not necessarily an indication that a chemical is recalcitrant or that it will be persistent in the environment. In contrast, inherent biodegradability tests use more favorable conditions to promote a high expected capacity for degradation, including the use of prolonged exposure periods and a low ratio of test substance to inoculum biomass. Passing this type of test indicates that a substance is inherently biodegradable but does not provide evidence for ready biodegradation. The available data included tests for both ready biodegradation and inherent biodegradation.

Tripropylene glycol was tested in three aerobic ready tests (OECD 301C, OECD 301B and OECD 301D) that reported <5% degradation over 28-day incubation periods, indicating that it is not readily biodegradable (OECD, 1994; Reported to the ECHA database, 1993a, 1991b). However, in another OECD 301D test, tripropylene glycol reached 69% O_2 consumption after 28 days and just missed the 10-day window criterion at 59% in 11 days under aerobic conditions (Reported to the ECHA

database, 1991a). In addition, both dipropylene glycol and tripropylene glycol reached ≥81% O_2 consumption after 28 days under aerobic conditions in the OECD 301F test, meeting the criteria for ready biodegradation but not meeting the 10-day window (Reported to the ECHA database, 2007a, c, 1994c). These data suggest that tripropylene glycol is aerobically biodegradable and may be readily biodegradable under the right conditions. Results from additional aerobic studies, including the inherent biodegradability test OECD 302A and a seawater biodegradability test (OECD 306) on dipropylene glycol provide further support that tripropylene glycol has the capacity to biodegrade under environmental conditions (Reported to the ECHA database, 2007d, 1994c). Furthermore, the microbial inhibition tests on tripropylene glycol and dipropylene glycol indicate that these substances are non-toxic to microbial populations found in sewage treatment plants (Reported to the ECHA database, 2010c, 1992b).

Based on the weight of scientific evidence, the data suggest 1,1'-dimethyldiethylene glycol is expected to biodegrade under aerobic conditions. Although under some test conditions this chemical may not meet the benchmark for ready biodegradation, both ready and inherent biodegradation of these substances has been demonstrated using a variety of standard and non-standard test methods.

Experimental data determined to be of adequate quality[36] on 1,1'-dimethyldiethylene glycol or closely related analogs were not reasonably available for the assessment of anaerobic biodegradation potential. Though BIOWIN modeling did not predict this chemical to anaerobically biodegrade quickly, these results do not indicate this chemical would not anaerobically biodegrade. The method used in the BIOWIN model is the ISO 11734 anaerobic test which measures methanogenic anaerobic biodegradation, one of several known pathways in anoxic environments. Other pathways include manganese and iron reduction, sulfate-reducing microorganisms, and halorespiring bacteria (Ghattas et al. 2017[37]). For 1,1'-dimethyldiethylene glycol, the chemical contains degradable functional groups such as primary alcohols and propylene glycol. For example, based on evidence for propylene glycol, EPA expects 1'1-dimethyldiethylene glycol could anaerobically biodegrade via methanogenic fermentation following a disproportionation reaction, forming propionate and n-propanol. These fermentation products would then be degraded via well-documented anaerobic oxidation reactions. In a serum bottle test using acclimated sludge, propylene glycol completely degraded to methane after 45 days (Veltman et al., 1998[38]). Additionally, the primary alcohol functional groups could convert to carboxylic acid under methanogenic conditions (Ghattas et al., 2017). While EPA cannot be certain of the rate at which these anerobic pathways may occur, this information supports the potential for 1,1'-dimethyldiethylene glycol to anaerobically biodegrade. In addition, 1'1-dimethyldiethylene glycol's low-hazard results for environmental and mammalian toxicity and evidence of aerobic biodegradation

[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 "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.

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

[38] Veltman, S., Schoenberg, M., and Switzenbaum, M.S. (1998) Alcohol and acid formation during the anaerobic decomposition of propylene glycol under methanogenic conditions. Biodegradation, 9 (2): 113-118. Available at: https://link.springer.com/article/10.1023%2FA%3A1008352502493#citeas.

provide sufficient information to indicate low concern for this chemical if present in anaerobic environments.

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 0.9 using the Estimation Programs Interface (EPI) Suite models,[39] EPA has sufficient information to indicate 1,1'-dimethyldiethylene glycol has low potential for bioaccumulation in the environment based on the low concern benchmark of less than 1000.

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

7. Exposure Characterization

EPA considered reasonably available information on exposure for 1,1'-dimethyldiethylene glycol. In general, there is limited information on exposure for low-hazard chemicals. EPA determined the CDR database and certain other sources of 1,1'-dimethyldiethylene glycol use information are sources of information relevant to 1,1'-dimethyldiethylene glycol's exposure potential. 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 also consulted sources of use information from other databases and public sources (listed in Table A.2). EPA used these sources only where they augmented information from the CDR database to inform intended, known, or reasonably foreseen uses (Section 5).

As shown in Tables 3 and A.3, 1,1'-dimethyldiethylene glycol is used in processing (incorporation into formulation, mixture or reaction) for plastics product manufacturing, detergents, cleaning compounds, and toilet preparation manufacturing. It is also used in industrial applications, such as construction and building materials, and consumer and commercial applications including air care products; cleaning and furnishing care products; laundry and dishwashing products; plastic and rubber products; arts and crafts; and toys, among others. 1,1'-Dimethyldiethylene glycol may have other uses, as shown in Table 3. 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, consumers, and infants and children.

7.1 Production Volume Information

Production volume information for 1,1'-dimethyldiethylene glycol is based on an analysis of CDR data reported from 1986 to 2015.[40] In the 1986 reporting year, aggregate production volume for 1,1'-dimethyldiethylene glycol was between 1,000,000 and 10,000,000 lbs. and in 1990, between 50,000,000 and 100,000,000 lbs. From the 1994 to 2002 reporting years, aggregate production volume for 1,1'-dimethyldiethylene glycol was between 10,000 and 500,000 lbs., and for the 2011 reporting year, the exact amount is available, at 146,990 lbs. Production reached a high of 1,000,000 to <10,000,000 lbs. in 2012; however, it has remained stable within the range of 500,000 to <1,000,000 lbs. from 2013-2015.

7.2 Exposures to the Environment

EPA expects most exposures to the environment to occur during the manufacture, import, processing, and industrial, commercial, and consumer uses of 1,1'-dimethyldiethylene glycol. Exposure is also reasonably foreseen from other conditions of use, such as distribution and disposal. These activities could result in releases of 1,1'-dimethyldiethylene glycol to media including surface water, landfills, and air.

[40] 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.

EPA expects high levels of removal of 1,1'-dimethyldiethylene glycol 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, 1,1'-dimethyldiethylene glycol is expected to have low persistence (aerobic biodegradation is 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 break down, reducing exposure to aquatic organisms in the water column and groundwater sources of drinking water, including well water. Based on the estimated log K_{oc} (Table 2 of Section 3), 1,1'-dimethyldiethylene glycol is expected to have negligible adsorption to sediment, reducing the potential for toxicity to benthic organisms. Further, 1,1'-dimethyldiethylene glycol's biodegradability during treatment processes will reduce the exposure potential to aquatic organisms.

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

If incineration releases during manufacturing and processing occur, EPA expects significant degradation of 1,1'-dimethyldiethylene glycol 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 1,1'-dimethyldiethylene glycol from the potential environmental releases described above. Air exposure is unlikely from incineration. If 1,1'diemthyldiethylene glycol is present in the air from volatilization, it is expected to be reduced because of its short atmospheric half-life of about 4 hours (see Table 2 in Section 3). With the exception of time immediately following a release, 1,1'-dimethyldiethylene glycol is unlikely to be present in surface water because it will degrade (discussed in Section 6.3.1), reducing the potential for the general population to be exposed by oral ingestion or dermal exposure. Further, given the low bioaccumulation or bioconcentration potential of 1,1'-dimethyldiethylene glycol, oral exposure to 1,1'-dimethyldiethylene glycol via fish ingestion is unlikely.

7.4 Exposures to Potentially Exposed or Susceptible Subpopulations

EPA identified workers, consumers, and infants and children as potentially exposed or susceptible subpopulations based on greater exposure to 1,1'-dimethyldiethylene glycol than the general population during manufacturing, processing, distribution, use and disposal. EPA identified infants and children (including any adults working closely with them) as a population that may experience greater exposure to 1,1'-dimethyldiethylene glycol than the general population during use of hobby products, toys, and baby mattresses and pillows. EPA also identified consumers as a population that may experience greater exposure to 1,1'-dimethyldiethylene glycol than the general population through use of printing inks, cleaning and furnishing care products, laundry and dishwashing products, air care products, and décor candles, for example.

7.4.1 Exposures to Workers

Based on its reported physical form and measured melting point (Table 2), 1,1'-dimethyldiethylene glycol is a liquid under ambient conditions. Based on 1,1'-dimethyldiethylene glycol's conditions of use, 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), 1,1'-dimethyldiethylene glycol is expected to be volatile at ambient temperatures, and therefore workers

may be exposed through inhalation of vapors. If 1,1'-dimethyldiethylene glycol is in a dilute form, the estimated Henry's Law constant for 1,1'-dimethyldiethylene glycol suggests volatilization from water and aqueous solutions is expected to be minimal. Workers may be exposed to 1,1'-dimethyldiethylene glycol in manufacturing, processing, distribution, use, and disposal.

7.4.2 Exposures to Consumers

Consumers could be exposed to 1,1'-dimethyldiethylene glycol through use of printing inks, cleaning and furnishing care products, laundry and dishwashing products, air care products, décor candles, and other products. For all these uses, if dermal contact does occur, 1,1'-dimethyldiethylene glycol is expected to have minimal absorption through the skin based on its molecular weight, water solubility and partitioning coefficients (Section 3) and experimental data (Section 6.1.1). If the chemical is in an aerosol product and inhalation exposure occurs, 1,1'-dimethyldiethylene glycol's absorption from the lungs is likely. 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). 1,1'-Dimethyldiethylene glycol is expected to be rapidly metabolized and excreted, further reducing the duration of exposure.

7.4.3 Exposures to Infants and Children

Children may be potentially exposed to 1,1'-dimethyldiethylene glycol through the use of hobby products, such as marker pens and toys, as noted in Table 3 (CPCat, 2019). In 2006, the Danish Environmental Protection Agency conducted a survey of the following types of children's hobby products: marker pens, glitter glue, acrylic paint, and shrink plastic. The initial screening detected over 70 chemicals, with 1,1'-dimethyldiethylene glycol detected in 3 of 26 marker pens; the chemical was not found in the other types of hobby products. The Danish EPA prioritized quantifying chemicals associated with hazardous effects, such as carcinogens, mutagens, and reproductive toxicants and allergenic substances. The amount of 1,1'-dimethyldiethylene glycol in the marker pens was not quantitatively analyzed because of its low-concern for hazard (Danish EPA, 2008a). In a survey conducted from 2013 to 2014 on children's toys by the Danish EPA, 1,1'-dimethyldiethylene glycol was detected in toy slime (at 5 mg/kg) but no other types of toys (Danish EPA, 2015)

As noted in Table 3 (CPCat, 2019), infants may also be exposed to 1,1'-dimethyldiethylene glycol via baby products. A 2008 survey by the Danish EPA investigated chemicals in the following types of baby products: pillows for baby feeding; baby carriers; nursing pillows and cushions with different covers and stuffing; baby mattresses with foam stuffing; aprons to perambulators; and disposable foam washcloths. 1,1'-Dimethyldiethylene glycol was detected in the foam of a baby mattress (at 56 μg/g) and the outer cover (cotton with printing) of a pillow for baby feeding (at 19 μg/g); the chemical was not detected in any of the other type of baby products investigated (Danish EPA, 2008b).

When children use marker pens and slime, skin contact is likely. When infants are placed on pillows for baby feeding, skin contact with 1,1'-dimethyldiethylene glycol is possible if the chemical is present in the outer cover. The same is true for baby mattresses if 1,1'-dimethyldiethylene glycol migrates from the foam to the surface. However, 1,1'-dimethyldiethylene glycol is expected to be poorly absorbed through the skin given its molecular weight, water solubility, and partitioning coefficients (Section 3) and experimental evidence on analogs (6.1.1). Based on the predicted Henry's

Law constant (Section 3), 1,1'-dimethyldiethylene glycol's volatilization from water and aqueous solutions is expected to be minimal, which is relevant for marker pens and toy slime, reducing inhalation exposures to children. While using these products, children may rub their eyes or incidentally ingest the product. Similarly, when infants are placed on baby mattresses or pillows for feedings, they may orally ingest the chemical if mouthing these products or sucking their fingers. If ingested, 1,1'-dimethyldiethylene glycol is expected to be rapidly metabolized and excreted, further reducing the duration of exposure. Therefore, EPA expects the exposures to 1,1'-dimethyldiethylene glycol through use of these products to be low.

EPA did not find information on the presence or concentration of 1,1'-dimethyldiethylene glycol in children's and baby products from sources beyond this Danish EPA study. EPA assumes that the hobby products, toys, baby mattresses, and pillows used for feeding tested by the Danish EPA are similar to products sold in the U.S., or that similar products and uses are reasonably foreseeable.

7.5 References

Danish EPA. (2008a). Survey and health assessment of chemical substances in hobby products for children. Retrieved from https://www2.mst.dk/udgiv/publications/2008/978-87-7052-763-7/pdf/978-87-7052-764-4.pdf

Danish EPA. (2008b). Survey, emission and health assessment of chemical substances in baby products https://www2.mst.dk/udgiv/publications/2008/978-87-7052-717-0/pdf/978-87-7052-718-7.pdf

Danish EPA. (2015). CMR Substances in Toys – Market Surveillance and Risk Assessment. Retrieved from https://www2.mst.dk/Udgiv/publications/2015/10/978-87-93352-79-7.pdf

8. Summary of Findings

EPA has used reasonably available information on the following statutory and regulatory criteria and considerations to screen 1,1'-dimethyldiethylene glycol against each of the priority designation considerations in 40 CFR 702.9(a), discussed individually in this section, under its conditions of use:

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

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

8.1 Hazard and Exposure Potential of the Chemical Substance

Approach: EPA evaluated the hazard and exposure potential of 1,1'-dimethyldiethylene glycol. EPA used this information to inform its determination of whether 1,1'-dimethyldiethylene glycol meets the statutory criteria and considerations for final designation as a low-priority substance.

- **Hazard potential:**

For 1,1'-dimethyldiethylene glycol's hazard profile, 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 the low-concern benchmarks. EPA found that 1,1'-dimethyldiethylene glycol is of low concern for human health and environmental hazard across the range of endpoints in this low-concern criteria.

- **Exposure potential:**

To understand exposure potential, EPA gathered information on physical-chemical properties, production volumes, and the types of exposures likely to be faced by workers, the general population,

consumers, and infants and children (discussed in Sections 3 and 7). EPA also gathered information on environmental releases. EPA identified workers, the general population, consumers, infants and children, and the environment as most likely to experience exposures. EPA determined that while the general population, consumers, children and workers may be exposed to 1,1'-dimethyldiethylene glycol, exposure by the dermal pathway is limited by 1,1'-dimethyldiethylene glycol's physical-chemical properties. If ingestion occurs, 1,1'-dimethyldiethylene glycol is expected to be metabolized and excreted, reducing the duration of exposure. Inhalation of 1,1'-dimethyldiethylene glycol in dilute products is expected to be minimal; however, workers may be exposed to vapors of neat 1,1'diemthyldiethylene glycol. If 1,1'-dimethyldiethylene glycol is released into the environment, its exposure potential will be reduced through biodegradation under aerobic conditions. EPA found that 1,1'-dimethyldiethylene glycol is of low concern for human and environmental exposure given the low hazard nature of this chemical substance.

Rationale: EPA determined that while workers, consumers, and infants and children may be exposed to 1,1'-dimethyldiethylene glycol during processing, manufacturing, distribution, use, or disposal, these exposures do not pose a significant risk because of the chemical's low-hazard results across a range of endpoints (discussed in Section 6). In summary, the concern for exposure is mitigated by the low-hazard profile of this chemical.

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

8.2 Persistence and Bioaccumulation

Approach: EPA has evaluated both the persistence and bioaccumulation potential of 1,1'-dimethyldiethylene glycol 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: As discussed in Section 6.3.1, EPA predicts 1,1'-dimethyldiethylene glycol will have a half-life less than 60 days. Given the low toxicity concern for this chemical, the low-concern criteria require that the chemical not produce degradation products of concern and have a half-life less than 60 days (Section 6.3.1). The available biodegradation results meet the low concern benchmark and suggest this chemical has low potential for persistence. Additionally, EPA's EPI Suite models indicate a low potential for bioaccumulation (Section 6.3.2).

Conclusion: Based on an initial screen of reasonably available information on persistence and bioaccumulation, EPA concludes that the screening-level review under 40 CFR 702.9(a)(2) does not support a finding that 1,1'-dimethyldiethylene glycol meets the standard for a high-priority substance. The reasonably available persistence and bioaccumulation information described above provides sufficient information to support this finding.

8.3 Potentially Exposed or Susceptible Subpopulations

Approach: TSCA Section 3(12) states that the "term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, or the elderly." EPA identified workers engaged in the manufacturing, processing, distribution, and disposal of 1,1'-dimethyldiethylene glycol, as well as consumers, infants and children, as potentially exposed or susceptible subpopulations (described in more detail in Section 7). EPA also identified infants and children (and any adults working closely with children) as a population that may experience greater exposure to 1,1'-dimethyldiethylene glycol than the general population during use of hobby materials such as marker pens, toys such as toy slime, and baby mattresses and pillows. Consumers are also a potentially exposed subpopulation because of their use of products such as printing inks, cleaning and furnishing care products, laundry and dishwashing products, air care products, décor candles, and other products.

Rationale: EPA did not identify hazard effects for this chemical that would make any population susceptible. EPA expects workers, consumers, and infants and children to have a higher exposure to 1,1'-dimethyldiethylene glycol than the general population. Higher exposure to children could result from use of products such as marker pens and toy slime containing 1,1'-dimethyldiethylene glycol, which might lead to inadvertent eye contact. Similarly, infants may have higher exposure to 1,1'-dimethyldiethylene glycol, and inadvertent eye contact with the chemical, from use of baby mattresses and pillows. Children and infants could also be exposed to 1,1'-dimethyldiethylene glycol via ingestion while using or teething these products. Because of the chemical's low-concern hazard properties, this exposure does not pose a significant increase in risk for children and infants.

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 1,1'-dimethyldiethylene meets the standard for a high-priority substance. The conditions of use could result in increased exposures to certain populations. Even in light of this finding, the consistently low-concern hazard profile of 1,1'-dimethyldiethylene glycol 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 1,1'-dimethyldiethylene glycol 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).

Rationale: In terms of health hazards, 1,1'-dimethyldiethylene glycol 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, 1,1'-dimethyldiethylene glycol is expected to be water soluble (see Section 3) and not expected to persist (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 1,1'-dimethyldiethylene glycol is unlikely to partition into sediment, predicted to biodegrade under aerobic conditions (see Section 3), and unlikely to bioaccumulate (see Section 6), minimizing the likelihood that the chemical would be present in sediment or groundwater to pose a longer-term drinking water contamination threat. Further, as explained in Section 6.1.3, repeated exposures of mice and rats to dipropylene glycol, a closely-related analog, through the drinking water exposure pathway indicate low concern for exposure through drinking water to this chemical.

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, 1,1'-dimethyldiethylene glycol would degrade in aerobic environments (see Section 6). Together, these factors mean that any exposures to this chemical through drinking water sources would be short-lived, and that if ingestion were to take place, concern for adverse health effects would be low.

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

Rationale: EPA evaluated the conditions of use of 1,1'-dimethyldiethylene glycol (see Section 5 and Appendix A) and found it to have a broad range of conditions of use.

EPA expects that even if the conditions of use were to expand beyond activities that are 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 1,1'-dimethyldiethylene glycol'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 1,1'-dimethyldiethylene glycol meets the standard for a high-priority substance, based on its low-hazard profile under the current conditions of use. EPA concludes that even if conditions of use broaden, resulting in an increase in the frequency or amount of exposures, the analysis conducted to support the screening-level review under 40 CFR 702.9(a)(5) would not change significantly. In particular, the analysis of concern for hazard, which forms an important basis for EPA's findings, would not be impacted by a change in conditions of use. Therefore, such changes would not support a finding that 1,1'-dimethyldiethylene glycol 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 1,1'-dimethyldiethylene glycol (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 1,1'-dimethyldiethylene glycol as a low-priority substance could result in increased use and higher production volumes. EPA expects, however, that any changes in 1,1'-dimethyldiethylene glycol's production volume would not alter the Agency's assessment of low concern given the chemical's low-hazard profile. EPA bases this expectation on 1,1'-dimethyldiethylene glycol's consistently low-concern hazard characteristics across the spectrum of hazard endpoints. This expectation would apply, even with a significant change in the volume of the chemical manufactured or processed and resultant increased exposures.

Conclusion: Based on this screening criteria under 40 CFR 702.9(a)(6), EPA concludes that even if production volumes increase, resulting in an increase in the frequency or level of exposure, 1,1'-dimethyldiethylene glycol 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 1,1'-dimethyldiethylene glycol as a low-priority substance.

9. Final Designation

Based on a risk-based screening-level review of the chemical substance and relevant information received from the public and other information as appropriate and consistent with TSCA section 26(h), (i) and (j), EPA concludes that 1,1'-dimethyldiethylene glycol 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 1,1'-dimethyldiethylene glycol as a low-priority substance.

Appendix A: Conditions of Use Characterization

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

A.1 CDR Manufacturers and Production Volume

The Chemical Data Reporting (CDR) rule (previously known as the Inventory Update Rule, or IUR), under TSCA section 8, requires manufacturers (including importers) to report information on the chemical substances they produce domestically or import into the U.S., generally above a reporting threshold of 25,000 lb. per site per year. According to the 2016 CDR database, 2 companies manufactured or imported 1,1'-dimethyldiethylene glycol at 3 sites for reporting year 2015.

Table presents the historic production volume of 1,1'-dimethyldiethylene glycol from the CDR from 1986-2015. In the 1986 reporting year, aggregate production volume for 1,1'-dimethyldiethylene glycol was between 1,000,000 and 10,000,000 lbs. and in 1990, between 50,000,000 and 100,000,000 lbs. From the 1994 to 2002 reporting years, aggregate production volume for 1,1'-dimethyldiethylene glycol was between 10,000 and 500,000 lbs., and for the 2011 reporting year, the exact amount is available, at 146,990 lbs. Production reached a high of 1,000,000 - <10,000,000 lbs. in 2012, however has remained stable within the range of 500,000 - <1,000,000 lbs. from 2013-2015.

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

1986	1990	1994	1998	2002	2006	2011	2012	2013	2014	2015
1M – 10M	50M – 100M	10K – 500K	10K – 500K	10K – 500K	1M – 10M	146,990	Withheld	500K - <1M	500K - <1M	500K - <1M

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

Note(s):
K = Thousands; M = Million

A.2 Uses

A.2.1 Methods for Uses Table

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

Table A.2: Sources Searched for Uses of 1,1'-Dimethyldiethylene Glycol

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)	110-98-5	No
Canada Chemicals Management Plan information sheets	Government of Canada (2018)	1,1'-dimethyldiethylene glycol; 1,1'-oxydi-2-propanol	No
Chemical and Product Categories (CPCat)	CPCat (2019)	110-98-5	Yes
ChemView [2]	EPA (2018a)	110-98-5	Yes
Children's Safe Product Act Reported Data	Washington State Dept. of Ecology (2018)	110-98-5	No
Consumer Product Information Database (CPID)	DeLima Associates (2018)	110-98-5	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	No
Datamyne	Descartes Datamyne (2018)	1,1'-dimethyldiethylene glycol; 1,1'-oxydi-2-propanol	No
DrugBank	DrugBank (2018b)	110-98-5	No
European Chemicals Agency (ECHA) Registration Dossier	ECHA (2018a; 2018b)	110-98-5	No
eChemPortal [2]	OECD (2018)	110-98-5	No
Envirofacts [2]	EPA (2018b)	110-98-5	No
Functional Use Database (FUse)	EPA (2017a)	110-98-5	Yes
Kirk-Othmer Encyclopedia of Chemical Technology	Kirk-Othmer (2006)	1,1'-dimethyldiethylene glycol; 1,1'-oxydi-2-propanol	No
Non-Confidential 2016 Chemical Data Reporting (CDR)	EPA (2017b)	110-98-5	Yes
PubChem Compound	Kim et al. (2016)	110-98-5	Yes

Table A.2: Sources Searched for Uses of 1,1'-Dimethyldiethylene Glycol			
Title	**Author and Year**	**Search Term(s)**	**Found Use Information? [1]**
Safer Chemical Ingredients List (SCIL)	EPA (2018d)	110-98-5	Yes
Synapse Information Resources [2]	Synapse Information Resources (2009)	1,1'-dimethyldiethylene glycol	Yes
Resource Conservation and Recovery Act (RCRA)	EPA (2018c)	1,1'-dimethyldiethylene glycol; 1,1'-oxydi-2-propanol	No
Scorecard: The Pollution Information Site	GoodGuide (2011b)	110-98-5	No
Skin Deep Cosmetics Database	EWG (2018a, 2018b)	Uses for CAS RN 110-98-5 with the chemical name listed as "Dipropylene Glycol" are included in Table A.3. EWG did not have search results for CAS RN 25265-71-8 or "1,1'dimethyldiethylene glycol." 1,1'-Dimethyldiethylene glycol is one of the isomers present in dipropylene glycol; uses for dipropylene glycol are listed in Table A.3 since a specific use under dipropylene glycol or 1,1'-dimethyldiethylene glycol cannot be distinguished.	
Toxics Release Inventory (TRI)	EPA (2018e)	110-98-5	No
TOXNET [2]	NLM (2018a)	110-98-5	Yes
Ullmann's Encyclopedia of Industrial Chemistry	Ullmann's (2000)	1,1'-dimethyldiethylene glycol; 1,1'-oxydi-2-propanol	No
Additional Sources Identified from Reasonably Available Information			
Boscia	Boscia (2018)	Incidentally identified while researching details of this chemical's uses and products.	Yes
Cetaphil	Cetaphil (2018)		
CVS	CVS (2018)		
Dove	Dove (2018)		
The Dow Chemical Company	Dow (2009)		
Medline	Medline.com (2009)		
National Archives and Records Information	National Archives and Records Administration (2018)		
National Pesticide Information Retrieval System (NPIRS)	NPIRS (2018)		
Neutrogena	Neutrogena (2018a)		
Shiseido	Shiseido (2018)		
Skinfood	Skinfood (2018)		

Note(s):

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

The U.S. Patent and Trademark Office has an online database that shows no patents referencing "1,1'dimethyldiethylene glycol" (USPTO 2018b). 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 1,1'-dimethyldiethylene glycol were not included in Table A.3. Note that the uses in Table A.3 that are covered under TSCA are included in Section 5, Table 3 of this document.

A.2.2 Uses of 1,1'-Dimethyldiethylene Glycol

Table A.3: Uses of 1,1'-Dimethyldiethylene Glycol		
Use	**Expected Users**	**Description of Use and References**
TSCA Conditions of Use: Automotive and Engine		
Automotive care	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in the "maintenance and repairs of motor vehicles" and in polishing agents for automotive lacquers (car wax). CPCat also lists use in automotive care paints. Expected users are industrial based on CPCat's user classification.
Automotive fuel	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in the "retail sale of automotive fuel in specialized stores." Expected users are industrial based on CPCat's user classification.
Automotive manufacturing	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in the "manufacture of motor vehicles, trailers and semi-trailers." Expected users are industrial based on CPCat's user classification.
Hydraulic brake fluid	Unknown	Synapse Information Resources (2009) Synapse Information Resources lists the use of 1,1'-dimethyldiethylene glycol as a solvent in hydraulic brake fluid.
Windscreen washing agents	Unknown	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in automotive windscreen and window care washing agents. Expected users are unknown, due to the limited availability of information.

Table A.3: Uses of 1,1'-Dimethyldiethylene Glycol		
Use	**Expected Users**	**Description of Use and References**
TSCA Conditions of Use: Cleaning and Maintenance Products		
Air care products	Consumer, commercial	EPA (2017b); CPCat (2019); Zep Inc (2015) CDR shows the use of 1,1'-dimethyldiethylene glycol in air care products at concentrations of at least 90 percent by weight. CPCat lists the use of 1,1'-dimethyldiethylene glycol in "air cleaners and anti-odor agents (not filters)." 1,1'-dimethyldiethylene glycol is listed as an ingredient in an air sanitizer product currently available for consumer and commercial use. Expected users are based on CDR's consumer/commercial classification.
Cleaning and furnishing care products	Consumer, commercial	EPA (2017b); CPCat (2019) CDR shows the use of 1,1'-dimethyldiethylene glycol in cleaning and furnishing care products, further information on exact uses were not reported to CDR. CDR reported concentrations in these products of at least 1 percent but less than 30 percent by weight. CPCat lists the use of 1,1'-dimethyldiethylene glycol in cleaning and washing agents, including industrial cleaning activities. Expected users are based on CDR's consumer/commercial classification.
Degreasers	Unknown	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in degreasers, including cold degreasing, de-waxing, de-polishing. Expected users are unknown, due to the limited availability of information.
Detergents manufacturing	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in the "manufacture of soaps and detergents, cleaning and polishing." Expected users are industrial based on identification in CDR's industrial processing and use report.

Table A.3: Uses of 1,1'-Dimethyldiethylene Glycol		
Use	**Expected Users**	**Description of Use and References**
Floor wash agent	Consumer, commercial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in cleaning and washing agents for floors. Expected users are not listed, but expected to be consumer and commercial.
Furniture washing	Unknown	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in "varnishing and acid washing of furniture." Expected users are unknown, due to the limited availability of information.
Industrial cleaning	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in industrial cleaning and washing, including specialized cleaning activities. Expected users are industrial based on CPCat's user classification.
Laundry and dishwashing products	Consumer, commercial	EPA (2017b) CDR shows the use of 1,1'-dimethyldiethylene glycol in laundry and dishwashing products at concentrations at less than 1 percent by weight. Expected users are based on CDR's consumer/commercial classification.
Lime deposit (calcium) remover	Unknown	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in lime deposit (calcium) removers. Expected users are unknown, due to the limited availability of information.

Table A.3: Uses of 1,1'-Dimethyldiethylene Glycol		
Use	**Expected Users**	**Description of Use and References**
Soap, cleaning compound, and toilet preparation manufacturing	Industrial	EPA (2017b) CDR shows the use of 1,1'-dimethyldiethylene glycol in processing, as an odor agent in soap, cleaning compound, and toilet preparation manufacturing Expected users are industrial based on identification in CDR's industrial processing and use report.
Textile detergent	Unknown	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in "washing agents for textiles (detergent)." Expected users are unknown, due to the limited availability of information.
TSCA Conditions of Use: Construction and Building		
Boat and ship buildings	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in the building and repairing of ships and boats. Expected users are industrial based on CPCat's user classification.
Construction	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in the construction of buildings, "general construction of buildings and civil engineering works," and in construction materials. Expected users are industrial based on CPCat's user classification.
Floor and wall material	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in floor and wall covering use as building materials. Expected users are industrial based on CPCat's user classification.

Table A.3: Uses of 1,1'-Dimethyldiethylene Glycol		
Use	**Expected Users**	**Description of Use and References**
Glass building materials	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in glass building materials. Expected users are not stated but are assumed to be industrial for glass building materials.
Wood manufacturing	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in the "manufacture of builders carpentry," and in the "manufacture of wood and of products of wood and cork" and "wooden goods to be used for buildings." CPCat also lists the use of 1,1'-dimethyldiethylene glycol as an impregnation material in wood. Expected users are industrial based on CPCat's user classification.
TSCA Conditions of Use: Food and Beverages		
Food and beverage service activities[1]	Unknown	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in food and beverage service activities. Expected users are unknown, due to the limited availability of information.
Food-contact coatings[1]	Unknown	Synapse Information Resources (2009) Synapse Information Resources lists the use of 1,1'-dimethyldiethylene glycol as a defoamer in food-contact coatings. Expected users are unknown, due to the limited availability of information.
Food-contact metallic manufacturing[1]	Industrial	Synapse Information Resources (2009) Synapse Information Resources lists the use of 1,1'-dimethyldiethylene glycol as a surface lubricant for the manufacturing of food-contact metallic articles. Expected users are unknown, due to the limited availability of information.

Table A.3: Uses of 1,1'-Dimethyldiethylene Glycol		
Use	**Expected Users**	**Description of Use and References**
Food packaging[1]	Unknown	Synapse Information Resources (2009) Synapse Information Resources lists the use of 1,1'-dimethyldiethylene glycol in food packaging adhesives and in paper/ paperboard in contact with fatty foods. Expected users are unknown, due to the limited availability of information.
TSCA Conditions of Use: Fuel		
Fuel additive	Unknown	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol as a fuel additive. No further information is available on the type of fuel in this use. Expected users are unknown, due to the limited availability of information.
Petroleum additive	Industrial	Synapse Information Resources (2009) Synapse Information Resources lists the use of 1,1'-dimethyldiethylene glycol as a petroleum anti-icing additive. Expected users are not listed but expected to be industrial for petroleum additives.
TSCA Conditions of Use: Industrial Uses		
Anti-foaming agents	Commercial, industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in changing fluid properties as an "anti-foaming agents, foam-reducing agents." Expected users are not listed, but are expected to be commercial and industrial for the use of anti-foaming agents.
Metal treatment and coating	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in the treatment and coating of metals. Expected users are industrial based on CPCat's user classification.

Table A.3: Uses of 1,1'-Dimethyldiethylene Glycol		
Use	**Expected Users**	**Description of Use and References**
Mining (except oil and gas) support activities	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in mining (except oil and gas) support activities. Expected users are not listed are assumed to be industrial for mining support activities.
TSCA Conditions of Use: Manufacturing		
Chemical manufacturing	Industrial	EPA (2017b); CPCat (2019) CDR shows the use of 1,1'-dimethyldiethylene glycol in processing, as an odor agent in "all other chemical product and preparation manufacturing." CPCat lists the use of 1,1'-dimethyldiethylene glycol in the "manufacture of chemicals and chemical products" and "other chemical products," including basic organic chemicals. Expected users are industrial based on identification in CDR's industrial processing and use report.
Electronic equipment manufacturing	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in the manufacture of electronic equipment. Expected users are industrial based on CPCat's user classification.
Fabricated metal products manufacturing	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in the "manufacture of fabricated metal products, except machinery." Expected users are industrial based on CPCat's user classification.
Furniture manufacturing	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in the manufacture of furniture. Expected users are industrial based on CPCat's user classification.

Table A.3: Uses of 1,1'-Dimethyldiethylene Glycol		
Use	**Expected Users**	**Description of Use and References**
Leather manufacturing	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in the "manufacture of leather and related products" and in the tanneries industry for leather bags and footwear. CPCat lists the use of 1,1'-dimethyldiethylene glycol in impregnation materials for leather. Expected users are industrial based on CPCat's user classification.
Machinery and equipment manufacturing	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in the manufacture of machinery and equipment. Expected users are industrial based on CPCat's user classification.
Paints, varnishes and coatings manufacturing	Consumer, commercial, industrial	CPCat (2019); Synapse Information Resources (2009) CPCat lists the use of 1,1'-dimethyldiethylene glycol in the manufacture of paints, varnishes, and similar coatings. CPCat also lists use in paints, lacquers and varnish products. Synapse Information Resources lists the use of 1,1'-dimethyldiethylene glycol as a surfactant in paints. Expected users are industrial based on CPCat's user classification. Consumer and commercial users are not listed but are assumed for uses of paints and varnish products.
Paper, pulp and paper product manufacturing	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in the manufacture of pulp, paper, and paper products. CPCat also lists the use of 1,1'-dimethyldiethylene glycol in impregnation materials for paper. Expected users are industrial based on CPCat's user classification.

Table A.3: Uses of 1,1'-Dimethyldiethylene Glycol		
Use	**Expected Users**	**Description of Use and References**
Perfumes manufacturing	Consumer, industrial	CPCat (2019); Synapse Information Resources (2009) CPCat lists the use of 1,1'-dimethyldiethylene glycol in the manufacture of perfumes and toilet preparations, including perfumes. CPCat also lists use in fragrances as an odor agent, including fragrances available for consumer use. Synapse Information Resources lists the use of 1,1'-dimethyldiethylene glycol as a fragrance fixative/ diluent, and as an aromatics extraction solvent. Expected users are consumer and industrial based on CPCat's user classification.
Plastics manufacturing	Industrial	EPA (2017b); CPCat (2019); Synapse Information Resources (2009) CDR shows the use of 1,1'-dimethyldiethylene glycol in processing, as a plasticizer in "plastics product manufacturing," and in processing, as an odor agent in "plastic material and resin manufacturing." CPCat lists the use of 1,1'-dimethyldiethylene glycol in the "manufacture of rubber and plastic products." Synapse Information Resources lists the use of 1,1'-dimethyldiethylene glycol comonomer and surfactant for unsaturated polyester resins, and in reinforced plastics. Expected users are industrial based on identification in CDR's industrial processing and use report.
Textile manufacturing	Consumer, industrial	CPCat (2019); Synapse Information Resources (2009) CPCat lists the use of 1,1'-dimethyldiethylene glycol in the manufacture of textiles, in "textile impregnation agents," and in textiles used in furniture including chair, seat upholstery and other consumer products. Synapse Information Resources lists the use of 1,1'-dimethyldiethylene glycol as a solvent in textile lubricants used for industrial purposes. Expected users are consumer and industrial based on CPCat's user classification.
Transport equipment manufacturing	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in the "manufacture of other transport equipment." Expected users are industrial based on CPCat's user classification.

Table A.3: Uses of 1,1'-Dimethyldiethylene Glycol		
Use	**Expected Users**	**Description of Use and References**
TSCA Conditions of Use: Miscellaneous Products		
Arts and crafts toys	Consumer	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in consumer arts and crafts toys for children. Expected users are consumer based on CPCat's user classification.
Baby products	Consumer	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in consumer baby products. No further information is provided on the specific baby products it is used in. Expected users are consumer based on CPCat's user classification.
Décor candle	Consumer	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in consumer incense products, including a décor candle. Expected users are consumer based on CPCat's user classification.
Plastic and rubber products	Consumer, commercial	EPA (2017b) CDR shows the use of 1,1'-dimethyldiethylene glycol in "plastic and rubber products not covered elsewhere" at concentrations of at least 30 percent but less than 60 percent by weight. Expected users are based on CDR's consumer/commercial classification.
Printing inks	Unknown	CPCat (2019); Synapse Information Resources (2009) CPCat lists the use of 1,1'-dimethyldiethylene glycol in serigraphy printing ink, also known as screen printing. Synapse Information Resources lists the use of 1,1'-dimethyldiethylene glycol as a solvent in printing inks. Expected users are unknown, due to the limited availability of information.

Table A.3: Uses of 1,1'-Dimethyldiethylene Glycol		
Use	**Expected Users**	**Description of Use and References**
Other Miscellaneous Uses		
Absorbents and adsorbents	Unknown	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in absorbents and adsorbents. Expected users are unknown, due to the limited availability of information.
Adhesive and binding agents	Unknown	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in adhesives and binding agents. Expected users are unknown, due to the limited availability of information.
Colorant	Unknown	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in colorants and coloring agents including dyestuff and pigments, Expected users are unknown, due to the limited availability of information.
Corrosion inhibitor	Unknown	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in corrosion inhibitors and rust inhibitors as a surface treatment. Expected users are unknown, due to the limited availability of information.
Polishing agent	Unknown	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in polishing agents. Expected users are unknown, due to the limited availability of information.

Table A.3: Uses of 1,1'-Dimethyldiethylene Glycol		
Use	**Expected Users**	**Description of Use and References**
Preservatives	Unknown	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in preservatives, conserving agents. Preservatives in food products is listed elsewhere. Expected users are unknown, due to the limited availability of information.
Non-TSCA Uses		
Agricultural pesticides	Unknown	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in pesticides for agricultural use. Expected users are unknown, due to the limited availability of information.
Bactericides	Unknown	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in bactericides, which function to kill bacteria, and bacteriostats, which aims to stop bacteria from reproducing. Expected users are unknown, due to the limited availability of information.
Biocides	Unknown	CPCat (2019); CPCat lists the use of 1,1'-dimethyldiethylene glycol in biocides for non-agricultural uses. Expected users are unknown, due to the limited availability of information.
Body wash	Consumer	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in body wash and body cleansers. Expected users are based on CPCat's user classification.
Deodorants and antiperspirants	Consumer	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in deodorants and antiperspirants. Expected users are based on CPCat's user classification.

Table A.3: Uses of 1,1'-Dimethyldiethylene Glycol		
Use	**Expected Users**	**Description of Use and References**
Disinfectants	Consumer, commercial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in disinfectants for cleaning and washing. Expected users are not listed but are expected to be consumer and commercial as they are stated for "public health area" use.
Facial treatments	Consumer	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in facial treatments. Expected users are based on CPCat's user classification.
Fungicides	Unknown	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in fungicides. Expected users are unknown, due to the limited availability of information.
Hair color	Consumer	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in hair color and hair dye. Expected users are based on CPCat's user classification.
Hair shampoo	Consumer	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in hair shampoos. Expected users are based on CPCat's user classification.
Hand soap and sanitizers	Consumer	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in hand soap and sanitizers for personal care use. Expected users are based on CPCat's user classification.

Table A.3: Uses of 1,1'-Dimethyldiethylene Glycol		
Use	**Expected Users**	**Description of Use and References**
Nail products	Consumer	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in cosmetic nail products. Expected users are not stated but are assumed to be consumer for nail products.
Permanent hair color	Consumer	DeLima Associates (2008, 2014) CPID lists the product for professional use, therefore expected users are consumer.
Pest control	Consumer	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in consumer pest control products. Expected users are consumer based on CPCat's user classification.
Preservative	Unknown	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in in-can preservatives. Expected users are unknown, due to the limited availability of information.
Shampoo manufacturing	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in the manufacture of hair shampoo. Expected users are industrial based on CPCat's user classification.
Slimicide	Industrial	CPCat (2019); National Archives and Records Administration (2018) CPCat lists the use of 1,1'-dimethyldiethylene glycol in slimicide. Slimicides are authorized for use in the manufacturing of paper and paperboard in the U.S. as an anti-microbial against slime-producing organisms. Expected users are not listed, but expected to be industrial as the use of slimicides are only permitted in manufacturing processes.

Table A.3: Uses of 1,1'-Dimethyldiethylene Glycol		
Use	**Expected Users**	**Description of Use and References**
Toothpaste manufacturing	Industrial	CPCat (2019) CPCat lists the use of 1,1'-dimethyldiethylene glycol in the manufacture of toothpaste. Expected users are industrial based on CPCat's user classification.
Children's Products CDR reports use in personal care products intended for children; CPID reports uses in baby products and arts and crafts.		
Recycling and Disposal In the 2016 CDR, two facilities reported that 1,1'-dimethyldiethylene glycol was not recycled (which could mean recycled, reprocessed, or reused). For one facility, recycling information was withheld. No further information about recycling or disposal was found.		
Note(s): 1. TSCA use based on the assumption that the chemical is used in the manufacturing of products and not intended to be a component of food.		

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Appendix B: Hazard Characterization

Table B.1: Human Health Hazard

ADME

Source	Exposure Route	Species & strain (if available)	Duration	Doses and replicate number	Effect	Study Details
4940508, 4940301, 3039551	Dermal *(in vitro)*	Human cadaver skin	24 hours	**Dose:** 768 µL undiluted test substance **Replicates:** 7 samples from 4 cadavers	The test material was considered a slow penetrant	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity: 99.9% • OECD Guideline 428 • GLP compliant **Results:** • Steady state penetration was 39.3 µg/cm^2-hour and the permeability coefficient was 3.85x10^{-5} cm/hour
3041958	Intravenous and oral	Dog	24 hours	**Doses:** 5000 mg/kg oral and 2000 mg/kg IV **Replicates:** 2 dogs	The test material is no longer detectable in blood after 24 hours	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity not reported • GLP compliance not reported
4940456, 4940388	Oral (gavage)	Fischer 344 rats	Single exposure, 24 hour observation	**Dose**: 48.2 mg/kg **Replicates:** 5 male rats	The test material is rapidly absorbed and distributed, and primarily excreted through urine. It is also extensively metabolized to dipropylene and monopropylene glycol and further oxidized to CO2	**Methods:** • Test substance reported as CASRN 24800-44-0 • Purity: 99.8% • GLP compliant **Results:** • Absorption: 91.4 ± 2.07 % of the dose administered was recovered indicating tripropylene glycol is rapidly absorbed • Distribution: The liver and kidney had the greatest amounts of tripropylene glycol • Metabolism: Tripropylene glycol is extensively metabolized. 5.8% of the

Table B.1: Human Health Hazard						
						dose was recovered as unmetabolized parent compound. Tripropylene glycol is metabolized to dipropylene and monopropylene glycol and further oxidized to CO_2 • Excretion: Dipropylene glycol was excreted primarily in the urine (52.3 ± 3.54%) and in exhaled breath (20.7±0.59%)
Acute Mammalian Toxicity						
Source	**Exposure Route**	**Species & strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
4951174	Oral (gavage)	Albino rats	Single exposure, 14 day observation	**Doses:** 10,000, 12,000, 14,000, 15,000, 16,000, 18,000, 20,000 and 25,000 mg/kg **Replicates:** 4-20 per group Groups: young male, male, adolescents, female adolescents, and male adults	**LD_{50}**: 12500 mg/kg (most conservative)	**Methods**: • Test substance reported as CASRN 110-98-5 • Purity not reported • GLP compliance not reported **Mortality:** • Young male rats: 10,000 mg/kg: 10%; 12,000 mg/kg: 10%; 14,000 mg/kg: 15%; 15,000 mg/kg: 60%; 16,000 mg/kg: (90%); LD_{50}: 14,8000 mg/kg • Adolescent male rats: 10,000 mg/kg: 10%; 12,000 mg/kg: 15%; 14,000 mg/kg: 75%; 15,000 mg/kg: 90%; 16,000 mg/kg: 100%; 18,000 mg/kg: 100%; 20,000 mg/kg: 90%; LD_{50}: 12,500 mg/kg • Adult male rats: 12,000 mg/kg: 10%; 14,000 mg/kg: 40%; 15,000 mg/kg: 80% LD_{50}: 14,200 mg/kg • Adolescent female rats: 12,000 mg/kg: 0%; 14,000 mg/kg: 0%; 16,000 mg/kg: 40%; 18,000 mg/kg: 80%; 20,000 mg/kg: 80%; 25,000 mg/kg: 100% LD_{50}: 16,500 mg/kg

Table B.1: Human Health Hazard						
4951174	Oral (gavage)	Guinea pigs	Single exposure, 14 day observation	**Doses**: 3,000, 4,000, 5,000, 6,000, 8,000, 10,000, 12,000, 15,000 and 20,000 mg/kg **Replicates:** 1-10 per group	**LD_{50}**: 10000 mg/kg	**Methods**: • Test substance reported as CASRN110-98-5 • Purity not reported • GLP compliance not reported **Morality:** • 3,000: 0%; 4,000: 20%; 5,000: 10%; 6,000: 30%; 8,000: 10%; 10,000: 50%; 12,000: 88%; 15,000: 100%; 20,000 mg/kg: 100%
4951207	Oral (gavage)	Albino rats	Single exposure, 14 day observation	**Doses:** 8815, 10,660, 12,710, 15,273, and 18,348 mg/kg **Replicates:** 5 per sex per dose	**LD_{50}**: 16195 mg/kg	**Methods**: • Test substance reported as CASRN110-98-5 • Purity not reported • GLP compliance not reported **Mortalities:** • 8815 mg/kg: 0/5 males, 0/5 females • 10,660 mg/kg: 2/5 males, 0/5 females • 12710 mg/kg: 0/5 males, 0/5 females • 15273 mg/kg: 2/5 males, 2/5 females • 18348 mg/kg: 4/5 males, 4/5 females
4940517	Inhalation	Rats	8 hour exposure, observed for 14 days	**Dose:** 0.083 mg/L **Replicates:** 6 animals	**LC_{50}** > 0.083 mg/L	**Methods:** • Test substance CASRN 24800-44-0 • Purity not reported • Pre-GLP compliance
4940443	Inhalation (aerosol)	Sprague-Dawley rats	4 hour exposure, observed for 14 days	**Dose:** 2.34 mg/L **Replicates:** 5 per sex	**LC_{50}** > 2.34 mg/L	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity: 100% • EPA OPP 81-3 • GLP compliant
4940519	Dermal	Albino rabbits	24 hour exposure, observed for 14 days	**Dose:** 16320 mg/kg **Replicates:** 5 males	**LD_{50}** > 16320 mg/kg	**Methods:** • Test substance reported as CASRN 24800-44-0 • Purity not reported • Pre-GLP compliance

Table B.1: Human Health Hazard						
4940453	Dermal	New Zealand White rabbits	24 hour exposure, observed for 14 days	**Dose:** 5010 mg/kg **Replicates:** 5 per sex	**LD_{50}** > 5010 mg/kg	**Methods:** • Test substance: CASRN 25265-71-8 • Purity: 100% • EPA OPP 81-2 • GLP compliant
Repeated Dose Toxicity						
Source	**Exposure Route**	**Species & strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
4940389, 4940514	Oral (gavage)	Sprague-Dawley rats	Male: 2 weeks prior to mating, 49 days total Females: 2 weeks prior to mating up to day 3 of lactation	**Doses:** 0, 8, 40, 200, and 1000 mg/kg-day **Replicates:** 12 per sex per group	**NOAEL**: 200 mg/kg-day **LOAEL**: 1000 mg/kg-day based on organ weight changes in parents	**Method:** • Test substance reported as CASRN 24800-44-0 • Purity > 98% • OECD Guideline 422 • GLP compliant
4940384, 4940445	Oral (drinking water)	B6C3F1 mice	2 years	**Doses:** Males: 0, 735, 1220, and 2390 mg/kg-day Females: 0, 575, 1040, and 1950 mg/kg-day **Replicates:** 50 per sex per dose	**NOAEL**: 1040 mg/kg-day **LOAEL**: 1950 mg/kg-day based on decreased mean body weight	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity: 99% • NTP Guideline • GLP compliant

Table B.1: Human Health Hazard						
4940466, 4940384	Oral (drinking water)	B6C3F1 mice	13 weeks	**Dose:** Males: 0, 715, 1350, 2620, 4790 and 11,000 mg/kg-day Females: 0, 1230, 2140, 4020, 7430 and 14700 mg/kg-day **Replicates:** 10 per sex per dose	**NOAEL**: 2620 mg/kg-day (male) **LOAEL**: 4790 mg/kg-day (male), based on increased liver weight	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity: 99% • NTP Guideline • GLP compliant **Endpoints:** • Mortality ○ 7,430 mg/kg-day females: (1/10) hypothermia ○ 11,000 mg/kg-day males: (3/10) dehydration ○ 14,700 mg/kg-day females: (1/10) dehydration
4940384, 4940465, 4940455	Oral (drinking water)	F344/N rats	2 years	**Doses:** Males: 0, 115, 470, and 3040 mg/kg-day Females: 0, 140, 530, and 2330 mg/kg-day **Replicates:** 50 per sex per dose	**NOAEL:** 115 mg/kg-day **LOAEL**: 470 mg/kg-day based on increased incidence of nephropathy, focal histiocytic, and focal granulomatous inflammation in male livers	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity: 99% • GLP compliance not reported

Table B.1: Human Health Hazard						
4940384, 4940462	Oral (drinking water)	F344/N rats	14 weeks (3 months)	**Doses:** Males: 0, 425, 890, 1840, 3890, and 12,800 mg/kg-day Females: 0, 460, 920, 1690, 3340, and 8950 mg/kg-day **Replicates:** 10 per sex per dose	**NOAEL:** 425 mg/kg-day **LOAEL:** 890 mg/kg-day based on relative liver weight	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity: 99% • GLP compliance not reported
Reproductive Toxicity						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
4940389, 4940514	Oral (gavage)	Sprague-Dawley rats	Male: 2 weeks prior to mating, 49 days total; Females: 2 weeks prior to mating up to day 3 of lactation	**Doses:** 0, 8, 40, 200, and 1000 mg/kg-day **Replicates:** 12 per sex per group	**NOAEL:** 200 mg/kg-day **LOAEL:** 1000 mg/kg-day based on organ weight changes in parents	**Method:** • Test substance reported as CASRN 24800-44-0 • Purity > 98% • OECD Guideline 422 • GLP compliant

Table B.1: Human Health Hazard						
Developmental Toxicity						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
4940450, 4440869, 4940388, 3041958	Oral (gavage)	Pregnant Sprague-Dawley rats	GD 6-15	**Doses:** 0, 800, 2000, and 5000 mg/kg-day **Replicates:** 20-27 per dose	**NOAEL:** 2000 mg/kg-day **LOAEL:** 5000 mg/kg-day based on decreased fetal body weight	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity > 96% • NTP Guideline • GLP compliance
4440871, 4940459, 4940388	Oral (gavage)	New Zealand White rabbit	GD 6-19	**Doses:** 0, 200, 400, 800, and 1200 mg/kg-day **Replicates:** 24 per group	**NOAEL:** 1200 mg/kg-day	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity > 96% • NTP protocol NTP-90-CTER-126 • GLP compliant
Cancer						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
4940448, , 4940384	Oral (drinking water)	Fischer 344 rats	2 years	**Doses:** Males: 0, 115, 470 and 3,040 mg/kg-day Females: 0, 140, 530 and 2,330 mg/kg-day **Replicates:** 50 per sex per dose	Negative	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity: 99% • NTP Guideline • GLP compliant

Table B.1: Human Health Hazard						
4940384, 4940448	Oral (drinking water)	B6C3F1 mice	2 years	**Doses:** Males: 735, 1220, and 2390 mg/kg-day; Females: 575, 1040, and 1950 mg/kg-day **Replicates:** 50 per sex per dose	Negative	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity: 99% • NTP Guideline • GLP compliant
Genotoxicity						
Source	**Test Type & endpoint**	**Species & strain (if available)**	**Metabolic activation**	**Doses and controls**	**Results**	**Study Details**
4940446, 4940384	Gene mutation (*in vitro)*	Salmonella typhimurium strains TA 97, TA98, TA100, TA 1535, TA 1538	With and without	**Doses:** 0, 100, 333, 1000, 3333 and 10000 µg/plate	Negative	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity > 99% • NTP Guideline • GLP compliant
4940463	Gene mutation (*in vitro)*	Mouse lymphoma L5178Y dells	With and without	**Doses:** 50, 100, 300, 500, 700, 1000, 2500 and 5000 µg/mL	Negative	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity not reported • OECD Guideline 476 • GLP compliant
4940467	Gene mutation (*in vitro)*	Salmonella typhimurium strains TA98, TA100, TA 1535, TA1537, TA 1538	With and without	**Doses**: 0.100, 0.316, 1.00, 3.16, 10.0, 31.6 and 100 µL/plate	Negative	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity: 99.9% • OECD Guideline 471 • GLP compliant

Table B.1: Human Health Hazard						
4940451, 4940388	Chromosomal aberrations (*in vivo)*	Mouse	N/A	**Doses:** 0, 500, 1000, and 2000 mg/kg **Replicates:** 6 per group	Negative	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity: 99.9% • OECD Guideline 474 • GLP Compliant
Sensitization						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
4940444, 4946133	Dermal patch	Human	2 day exposure, observed 7 days	Study 1 **Doses:** 1%, 2%, 5%, and 10% in **Replicates:** 34 patients Study 2 **Dose:** 10% in **Replicates:** 503 volunteers 212 Males 291 Females	Equivocal	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity > 96% • GLP compliance not reported **Results:** • 1 person had positive reaction (only to standard grade dipropylene glycol) • 488 subjects showed no reaction and 13 subjects showed equivocal reaction to standard grade substance • 480 subjects showed no reaction and 17 subjects showed equivocal reaction to cosmetic grade substance • Irritation was indicated in 2 analytical grade and 5 cosmetic grade volunteers

Table B.1: Human Health Hazard						
4940460	Dermal	Guinea pigs	6 hour exposure, induction repeated 3 times for 2 weeks	**Dose:** 0.5 mL **Replicates:** 10 animals (7 Males 3 Females)	Negative	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity: 100% • EPA OPP 81-6 • GLP compliant **Results:** • 1 animal displayed slight patchy erythema 24 hours after
3118622	Dermal patch	Humans	24 hour exposure, scored after 48 hours; repeated for 9 applications	**Dose:** 0.4 mL **Replicates:** 42 volunteers	Negative	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity not reported • Modified Draize Method • GLP compliance not reported
Irritation						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses**	**Effect**	**Study Details**
4940512	Dermal	Rabbits	24 hours	**Dose:** 0.01 mL of undiluted solution **Replicates:** 5 animals	Minimally irritating	**Methods** • Test substance reported as CASRN 24800-44-0 • Purity not reported • Pre-GLP compliance **Results:** • Mean irritation score was 2 out of 10 (with 1 = no irritation). Moderate capillary injection was observed on 4 rabbits
4940527	Dermal patch	Humans	24 hours	**Dose:** 0.2 mL of 25% solution **Replicates:** 33 volunteers	Negative	**Methods** • Test substance reported as CASRN 24800-44-0 • Purity not reported • Non-GLP compliant **Results:** • 2 volunteers had mild erythema at 0.5 hours which resolved by 24 hours

Table B.1: Human Health Hazard						
4940526	Dermal patch	Humans	Daily for 14 days	**Dose:** 0.2mL of 50% solution **Replicates:** 26 volunteers	Negative	**Methods** • Test substance reported as CASRN 24800-44-0 • Purity not reported • Non-GLP compliant • 1/ 26 subjects did not complete the due to reasons unrelated to exposure
4940447	Dermal	Humans	Daily for 14 days	**Doses:** 0.2 mL of 50% and 100% of test substance **Replicates:** 26 skin-sensitive volunteers	Negative	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity not specified • GLP compliance not reported **Results:** • One volunteer had a mildly irritating response (erythema) to 100% substance before day 4
4940461	Dermal	New Zealand White rabbit	4 hour exposure, observed for 72 hours	**Dose:** 0.5 mL **Replicates:** 3 per sex	Negative	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity: 100% • EPA OPP 81-5 • GLP compliant **Results:** • Very slight erythema observed in 1/6 animals within 45 min, but all test areas were normal for the remaining observation periods
4940458	Dermal patch	Human	24 hour exposure	**Dose:** 0.2 mL of 25% **Replicates:** 33 subjects	Mildly irritating	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity not reported • GLP compliance not reported **Results:** • At the 24-hour scoring, 4/33 subjects displayed mild erythema

Table B.1: Human Health Hazard						
3118622	Dermal	Albino rabbit	24 hour exposure, observed for 72 hour	**Dose:** 0.5 mL **Replicates:** 3 rabbits per group	Negative	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity not reported • Draize Method • GLP compliance not reported
4940453	Dermal	New Zealand White rabbit	24 hour exposure, observed for 14 day	**Dose:** 5010 mg/kg **Replicates**: 5 per sex	Negative	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity: 100% • EPA OPP 81-2 • GLP compliant **Results:** • Very slight irritation was observed in 5/10 animals 45 minutes after removal of patch, but all effects were fully reversible by 48 hours
4940449	Ocular	New Zealand White rabbit	Single exposure, 72 hour exposure	**Dose:** 0.1 mL **Replicates:** 3 per sex	Negative	**Method:** • Test substance reported as CASRN 25265-71-8 • Purity: 100% • EPA OPP 81-4 • GLP compliant **Results:** • 6/6 animals had conjunctival redness and 2/6 animals displayed chemosis after 1 hour, but these results were fully reversible by 24 hours

Table B.1: Human Health Hazard						
3118622	Ocular	Rabbits	Single exposure, observed for 7 days	**Dose:** 0.1 mL **Replicates:** 3 rabbits per group	Negative	**Method:** • Test substance reported as CASRN 25265-71-8 • Purity not reported • Draize Method • GLP compliance not reported **Results:** • Eye irritation did not differ between vehicle control and test material
4940520	Ocular	Rabbits	Single exposure, observed over 24 hours	**Dose:** 0.5 mL of undiluted solution **Replicates:** 5 rabbits	Negative	**Methods** • Test substance reported as CASRN 24800-44-0 • Purity not reported • Pre-GLP compliance **Results:** • The overall irritation score was 1 (trace or no injury) and was fully reversible. The test material was considered non-irritating
4940518	Ocular	New Zealand White rabbits	Single exposure, observed over 72 hours	**Dose:** 0.1 mL of undiluted solution **Replicates:** 2 animals	Negative	**Methods** • Test substance reported as CASRN 24800-44-0 • Purity=99.6% • OECD Guideline 405 • GLP compliant **Results:** • 2/2 animals had mild conjunctival redness, chemosis, and conjunctival discharge at the 1-hour scoring • All effects were reversible by 24 hours
4940513	Ocular	SkinEthic Human Corneal Epithelium Model (*in vitro*)	10 minutes	**Dose:** 30 µL of undiluted solution **Replicates:** 3 replicates	Negative	**Methods** • Test substance reported as CASRN 24800-44-0 • Purity: 99.6% • GLP compliant

Table B.1: Human Health Hazard						
Other						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses**	**Effect**	**Study Details**
4088550	Cell viability	Human embryonic stem cells (hESCs) and human adult pulmonary fibroblasts (hPF)	NA	**Doses:** 0.0001 M to 0.1 M	**NOAEL:** 0.00745M for hESCs; IC50: 0.04 M for hESCs and hPF	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity not reported • GLP compliance not reported **Results:** • In hESCs the estimated NOAEL was 0.00745M and the IC50 was 0.045M, only the highest concentration tested was significantly different from (vehicle) controls • The IC50 in hPF cells was identical (0.04M), but a reliable NOAEL could not be determined

Table B.2: Environmental Hazard					
Aquatic Toxicity: Experimental					
Source	**Species & strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
4940438	*Daphnia magna*	48 hours	**Dose:** 100 mg/L	**EC_{50}** > 100 mg/L	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity: 100% • EPA 540/9-82-024, EPA-540/9-85-005 and ASTM Standards E729-88a • GLP compliant
4940439	*Daphnia magna*	48 hours	**Doses:** 0, 12.5, 25, 50, and 100 mg/L	**EC_{50}** > 100 mg/L	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity: 99.6% • OECD Guideline 202 • GLP compliant

Table B.2: Environmental Hazard					
4940389, 4940442	*Oryzias latipes*	96 hours	**Doses:** 5 concentrations between 95-1000 mg/L (nominal) **Replicates:** 10 per group	**LC_{50}** > 1000 mg/L	**Methods:** • Test substance reported as CASRN 24800-44-0 • Purity: 97% • OECD Guideline 203 • Not GLP compliant
4940389, 4940433	*Daphnia magna*	24 hours	**Doses**: 5 concentrations between 10-1000 mg/L **Replicates:** 4 replicates per concentration, 5 organisms per replicates	**EC_{50}** > 1000 mg/L	**Methods:** • Test substance reported as CASRN 24800-44-0 • Purity: 97% • OECD Guideline 202 • Not GLP compliant
4940389	*Selenastrum capricornutum*	72 hours	**Doses:** 5 nominal concentrations 95-1000 mg/L	**EC_{50}** > 1000 mg/L	**Methods:** • Test substance reported as CASRN 24800-44-0 • Purity: 97% • OECD Guideline 201 • Not GLP compliant
Aquatic Toxicity: Estimated					
Model	**Duration**	**Species**	**Predicted Effect Level**	**Notes**	
ECOSAR v2.0 (Class: Neutral Organics)	96 hours	Freshwater fish	18000 mg/L	Physical properties used for estimation Log K_{ow} -0.46 (exp); water solubility 1000 mg/L; melting point -40°C SMILES: O(CC(O)C)CC(O)C	
ECOSAR v2.0 (Class: Neutral Organics)	48 hours	Daphnia magna	8100 mg/L	Physical properties used for estimation Log K_{ow} -0.46 (exp); water solubility 1000 mg/L; melting point -40°C SMILES: O(CC(O)C)CC(O)C	
ECOSAR v2.0 (Class: Neutral Organics)	72 hours	Green algae	2400 mg/L	Physical properties used for estimation Log K_{ow} -0.46 (exp); water solubility 1000 mg/L; melting point -40°C SMILES: O(CC(O)C)CC(O)C	
ECOSAR v2.0 (Class: Neutral Organics)	ChV	Freshwater fish	1300 mg/L	Physical properties used for estimation Log K_{ow} -0.46 (exp); water solubility 1000 mg/L; melting point -40°C SMILES: O(CC(O)C)CC(O)C	
ECOSAR v2.0 (Class: Neutral Organics)	ChV	Daphnia magna	420 mg/L	Physical properties used for estimation Log K_{ow} -0.46 (exp); water solubility 1000 mg/L; melting point -40°C SMILES: O(CC(O)C)CC(O)C	
ECOSAR v2.0 (Class: Neutral Organics)	ChV	Green algae	370 mg/L	Physical properties used for estimation Log K_{ow} -0.46 (exp); water solubility 1000 mg/L; melting point -40°C SMILES: O(CC(O)C)CC(O)C	

Table B.3: Fate					
Environmental Fate: Experimental					
Source	**Endpoint**	**Duration**	**Doses and number of replicates**	**Results**	**Study Details**
4940389	BOD	28 days	**Dose**: 100 mg/L	Not readily biodegradable	**Method:** • Test substance reported as CASRN 24800-44-0 • Purity not reported • OECD Guideline 301C • GLP compliant **Results:** • 0% degradation by TOC and 0-3% by GC after 28 days • 1-2% BOD degradation after 28 days
4940425	CO_2 evolution	28 days	NA	Not readily biodegradable	**Method:** • Test substance reported as CASRN 24800-44-0 • Purity: 95% • OECD Guideline 301B • GLP compliant **Results:** • 0% degradation by DOC after 28 days 4-5% degradation by CO_2 evolution after 28 days
4940426	O_2 consumption	28 days	NA	69% degradation after 28 days	**Method:** • Test substance reported as CASRN 24800-44-0 • Purity: 99.43% • OECD Guideline 301D • GLP compliant **Results:** • 59% in 11 days 69% degradation after 28 days
4940432	O_2 consumption, CO_2 consumption, DOC removal	28 days	**Dose:** 100 mg/L	Readily biodegradable	**Method:** • Test substance reported as CASRN 24800-44-0 • Purity: 99.9% • OECD Guideline 301F • GLP compliant **Results:** • 81.9% O_2 consumption, 61% CO_2 consumption, 91.7% DOC removal after 28 days

Table B.3: Fate					
					• 55.3% biodegradation within 10-day window
4940431	O_2 consumption	28 days	NA	Not readily biodegradable	**Method:** • Test substance reported as CASRN 24800-44-0 • Purity: 99.43% • OECD Guideline 301D • GLP compliant **Results:** • 0% degradation by O_2 consumption after 28day (below detection limit of <2.5% ThOD)
4940428	Aerobic seawater	64 days	**Dose:** 51.2 mg/L	• 46.1% DOC removal after 64 days • 33.5% CO_2 evolution after 62 days	**Method:** • Test substance reported as CASRN 24800-44-0 • Purity 99.4% • OECD Guideline 306 • GLP compliant
4946320	Sediment/Water	20 days	**Doses:** 5 and 10 mg/L	Inherently Biodegradable	**Method:** • Test substance reported as CASRN 24800-44-0 • Purity not reported • OECD Guideline 301E • GLP compliant **Endpoint:** • < 10% after 20 days with 10 mg/L dose • 100% biodegradation by day 16 with 5 mg/L • Authors suggest that oxidation products may be toxic to inoculum and TPG is inherently biodegradable
4940427	O_2 consumption, CO_2 evolution, DOC removal	28 days	**Dose:** 100 mg/L	Readily biodegradable	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity: 99.9% • OECD Guideline 301F • GLP compliant **Endpoints:** • O_2 consumption: 58.7% after 10 days, 84.4% after 28 days. • CO_2 evolution: 64.5% after 28 days.

Table B.3: Fate					
					DOC removal: 93.4% after 28 days.
1763085	BOD		**Doses:** 14-6816 mg/L	Insufficient 0_2 consumption	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity not reported • Standard methods (APHA 195) • GLP compliance not reported **Endpoints:** • BOD < 0.001 g/g using microbial seed from supernatant of settled raw sewage. • Insufficient 0_2 consumption
4940429	DOC removal using activated sludge inoculum	6 weeks	**Dose:** 18.5 mg/L	DOC removal 83.6% after 6 weeks	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity > 99.9% • OECD Guideline 301F or OECD Guideline 302A • GLP compliant **Endpoints:** • DOC removal 83.6% after 6 weeks • Biodegradation from days 10-42 of 82.5-84.7%
4940424	CO_2 evolution and BOD removal	64 days	**Dose:** 50.3 mg/L	DOC removal showed 23.6+/-0.3% degradation after 64 days CO_2 evolution showed 17.3+/-2.6% degradation after 62 days	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity: 99.4% • OECD Guideline 306 • GLP compliance not reported
4940437	Toxicity to microorganisms	3 hours	**Doses**: 10, 32, 100, 320 and 1000 mg/L	**NOEC**: 1000 mg/L	**Methods:** • Test substance reported as CASRN 24800-44-0 • Purity: 99.9% • OECD Guideline 209 • GLP compliant **Results:** • EC50 >1000 mg/L (nominal)

Table B.3: Fate					
4940441	Toxicity to microorganisms	18 hours	**Doses:** Range Finding: 0.1,1, 100, and 1000 mg/ L Main study: 1.95, 3.91, 7.81, 15.63, 31.25, 62.5, 125, 250, 500, and 1000 mg/L	**EC_{10}** > 1000 mg/L	**Methods:** • Test substance reported as CASRN 25265-71-8 • Purity: 99.9% • GLP compliant
Environmental Fate: Modelled					
Model	**Data Type**	**Endpoint**	**Predicted Endpoint**	**Notes**	
EPISuite v.4.11	Estimated	BAF	0.9		
EPISuite v.4.11	Estimated	BCF	3.16		
EPISuite v.4.11 (BIOWIN 7)	Estimated	Anaerobic biodegradation	Not predicted to biodegrade quickly under anaerobic conditions	Probability of 0.4055. Fragment representation is valid. Fast degradation is defined as predicted probability >0.5.	

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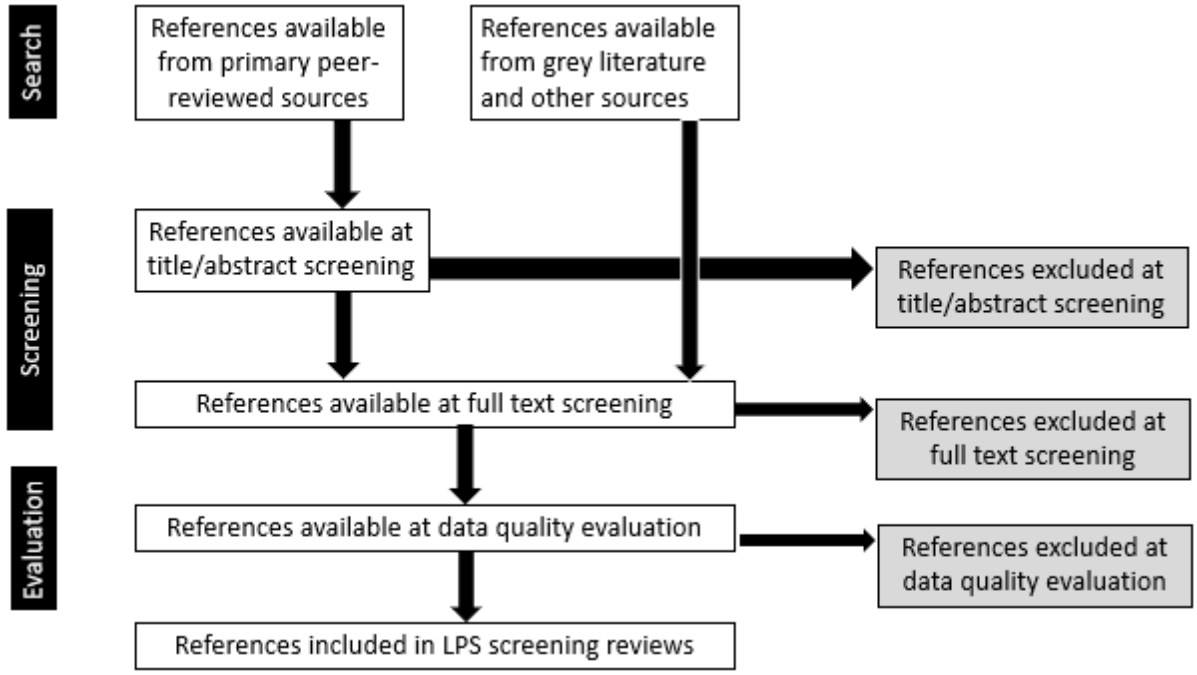
Appendix C: Literature Search Outcomes

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 1,1'-dimethyldiethylene glycol. Search outcomes and reference details are provided on the candidate's HERO[41] project page.

EPA created a fit-for-purpose process to transparently document the literature search and review[42] of available hazard and fate information for low-priority substance (LPS) candidates. References from peer-reviewed primary sources, grey sources,[43] 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



C.1.1 Search for Analog Data

To supplement the information on the candidate chemical, 1,1'-dimethyldiethylene glycol, the following LPS candidates were used as analogs for read-across: tripropylene glycol (CASRN 24800-44-0) and

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

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

[43] 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.

dipropylene glycol (CASRN 25265-71-8). For more details and justification on analogs, see section 6.1.1. Analogs were used to fill data gaps on endpoints for which 1,1'-dimethyldiethylene glycol lacked quality data, such as repeated dose and developmental toxicity, and to add to the weight of the scientific evidence. Analog references were searched, screened and evaluated using the same process as references on 1,1'-dimethyldiethylene glycol described above.[42] 1,1'-Dimethyldiethylene glycol and the two analogs mentioned above fall under the glycol cluster in HERO.

C.1.2 Search Terms and Results

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

Table C.1: Search Terms Used in Peer Reviewed Databases		
Discipline	**Database**	**Search terms**
Human Health	PubMed	25265-71-8[rn] OR 110-98-5[rn] OR 24800-44-0[rn] OR "((1-methyl-1,2-ethanediyl)bis(oxy))bispropanol"[tw] OR "((Methylethylene)bis(oxy))dipropanol"[tw] OR "1,1'-Dimethyldiethylene glycol"[tw] OR "1,1'-Oxybis(2-propanol)"[tw] OR "1,1'-Oxybis-2-propanol"[tw] OR "1,1'-Oxydi-2-propanol"[tw] OR "1,1'-Oxydipropan-2-ol"[tw] OR "2,2'-Dihydroxydipropyl ether"[tw] OR "2-(2-(2-Hydroxypropoxy)propoxy)-1-propanol"[tw] OR "2-Propanol, 1,1'-oxybis-"[tw] OR "2-Propanol, 1,1'-oxydi-"[tw] OR "4-Oxa-2,6-heptandiol"[tw] OR "4-Oxaheptane-2,6-diol"[tw] OR "ADK DPG-RF"[tw] OR "Bis(2-hydroxypropyl) ether"[tw] OR "Bis(3-hydroxypropyl)ether"[tw] OR "Diisopropylene glycol"[tw] OR "Dipropylene glycol"[tw] OR "DIPROPYLENEGLYCOL"[tw] OR "DIPROPYLENGLYKOL"[tw] OR "Dowanol DPG"[tw] OR "DPG-FC"[tw] OR "DPG-RF"[tw] OR "NIAX catalyst D-19"[tw] OR "oxidipropanol"[tw] OR "Oxybispropanol"[tw] OR "Oxydipropanol"[tw] OR "Propanol, ((1-methyl-1,2-ethanediyl)bis(oxy))bis-"[tw] OR "Propanol, oxybis-"[tw] OR "Tripropylene glycol"[tw]
	Toxline	(25265-71-8[rn] OR 110-98-5[rn] OR 24800-44-0[rn] OR "((1-methyl-1,2-ethanediyl)bis(oxy))bispropanol" OR "((Methylethylene)bis(oxy))dipropanol" OR "1,1'-Dimethyldiethylene glycol" OR "1,1'-Oxybis(2-propanol)" OR "1,1'-Oxybis-2-propanol" OR "1,1'-Oxydi-2-propanol" OR "1,1'-Oxydipropan-2-ol" OR "2,2'-Dihydroxydipropyl ether" OR "2-(2-(2-Hydroxypropoxy)propoxy)-1-propanol" OR "2-Propanol, 1,1'-oxybis-" OR "2-Propanol, 1,1'-oxydi-" OR "4-Oxa-2,6-heptandiol" OR "4-Oxaheptane-2,6-diol" OR "ADK DPG-RF" OR "Bis(2-hydroxypropyl) ether" OR "Bis(3-hydroxypropyl)ether" OR "Diisopropylene glycol" OR "Dipropylene glycol" OR "DIPROPYLENEGLYCOL" OR "DIPROPYLENGLYKOL" OR "Dowanol DPG" OR "DPG-FC" OR "DPG-RF" OR "NIAX catalyst D-19" OR "oxidipropanol" OR "Oxybispropanol" OR "Oxydipropanol" OR "Propanol, ((1-methyl-1,2-ethanediyl)bis(oxy))bis-" OR "Propanol, oxybis-" OR "Tripropylene glycol") AND (ANEUPL [org] OR BIOSIS [org] OR CIS [org] OR DART [org] OR EMIC [org] OR EPIDEM [org] OR FEDRIP [org] OR HEEP [org] OR HMTC [org] OR IPA [org] OR RISKLINE [org] OR MTGABS [org] OR NIOSH [org] OR NTIS [org] OR PESTAB [org] OR PPBIB [org]) AND NOT PubMed [org] AND NOT pubdart [org]
	TSCATS 1	(25265-71-8 [rn] OR 110-98-5 [rn] OR 24800-44-0 [rn]) AND (TSCATS [org]) AND NOT PubMed [org] AND NOT pubdart [org]
	WOS	TS=("25265-71-8" OR "110-98-5" OR "24800-44-0" OR "((1-methyl-1,2-ethanediyl)bis(oxy))bispropanol" OR "((Methylethylene)bis(oxy))dipropanol" OR "1,1'-Dimethyldiethylene glycol" OR "1,1'-Oxybis(2-propanol)" OR "1,1'-Oxybis-2-propanol" OR "1,1'-Oxydi-2-propanol" OR "1,1'-Oxydipropan-2-ol" OR "2,2'-Dihydroxydipropyl ether" OR "2-(2-(2-Hydroxypropoxy)propoxy)-1-propanol" OR "2-Propanol, 1,1'-oxybis-" OR "2-Propanol, 1,1'-oxydi-" OR "4-Oxa-2,6-heptandiol" OR "4-Oxaheptane-2,6-diol" OR "ADK DPG-RF" OR "Bis(2-hydroxypropyl) ether" OR "Bis(3-hydroxypropyl)ether" OR "Diisopropylene glycol" OR "Dipropylene glycol" OR "DIPROPYLENEGLYCOL" OR "DIPROPYLENGLYKOL" OR "Dowanol DPG" OR "DPG-FC" OR "DPG-RF" OR "NIAX catalyst D-19" OR "oxidipropanol" OR "Oxybispropanol" OR "Oxydipropanol" OR "Propanol, ((1-methyl-1,2-ethanediyl)bis(oxy))bis-" OR "Propanol, oxybis-" OR "Tripropylene glycol") Indexes=SCI-EXPANDED, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, CCR-EXPANDED, IC Timespan=All years
Environmental Hazard	WOS	Same as human health strategy synonyms only
	Toxline	Same as human health strategy synonyms only

Table C.1: Search Terms Used in Peer Reviewed Databases		
	TSCATS 1	Same as human health strategy CASRN only
	Proquest	TITLE=("25265-71-8" OR "1,1'-Oxybis 2-propanol" OR "1,1'-Oxybis-2-propanol" OR "1,1'-Oxydi-2-propanol" OR "1,1'-Oxydipropan-2-ol" OR "2-Propanol, 1,1'-oxybis-" OR "Bis 2-hydroxypropyl ether" OR "Dipropylene glycol" OR "DIPROPYLENEGLYCOL" OR "Propanol, oxybis-" OR "Tripropylene glycol") ABSTRACT=("25265-71-8" OR "1,1'-Oxybis 2-propanol" OR "1,1'-Oxybis-2-propanol" OR "1,1'-Oxydi-2-propanol" OR "1,1'-Oxydipropan-2-ol" OR "2-Propanol, 1,1'-oxybis-" OR "Bis 2-hydroxypropyl ether" OR "Dipropylene glycol" OR "DIPROPYLENEGLYCOL" OR "Propanol, oxybis-" OR "Tripropylene glycol") SUBJECT=("25265-71-8" OR "1,1'-Oxybis 2-propanol" OR "1,1'-Oxybis-2-propanol" OR "1,1'-Oxydi-2-propanol" OR "1,1'-Oxydipropan-2-ol" OR "2-Propanol, 1,1'-oxybis-" OR "Bis 2-hydroxypropyl ether" OR "Dipropylene glycol" OR "DIPROPYLENEGLYCOL" OR "Propanol, oxybis-" OR "Tripropylene glycol") ("110-98-5" OR "24800-44-0" OR "1-methyl-1,2-ethanediyl bis oxy bispropanol" OR "Methylethylene bis oxy dipropanol" OR "1,1'-Dimethyldiethylene glycol" OR "2,2'-Dihydroxydipropyl ether" OR "2- 2- 2-Hydroxypropoxy propoxy -1-propanol" OR "2-Propanol, 1,1'-oxydi-" OR "4-Oxa-2,6-heptandiol" OR "4-Oxaheptane-2,6-diol" OR "ADK DPG-RF" OR "Bis 3-hydroxypropyl ether" OR "Diisopropylene glycol" OR "DIPROPYLENGLYKOL" OR "Dowanol DPG" OR "DPG-FC" OR "DPG-RF" OR "NIAX catalyst D-19" OR "oxidipropanol" OR "Oxybispropanol" OR "Oxydipropanol" OR "Propanol, 1-methyl-1,2-ethanediyl bis oxy bis-")
Fate	WOS	Same as human health strategy synonyms only

Table C.2: Search Terms Used in Grey Literature and Additional Sources	
Chemical	**Search terms**
Glycol cluster (1,1'-Dimethyldiethylene glycol; dipropylene glycol, tripropylene glycol)	Searched as a string or individually depending on resource: "25265-71-8" OR "110-98-5" OR "24800-44-0" OR "Dipropylene glycol" OR "Dipropyleneglycol" OR "Propanol, oxybis-" OR "Tripropylene glycol"

After the search terms were applied, more than 620 references 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.[42] Of these, 71 references were included for data evaluation and used to support the designation of 1,1'-dimethyldiethylene glycol 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 1,1'-dimethyldiethylene glycol. 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[42] 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 1,1'-dimethyldiethylene glycol, EPA excluded a total of 539 references when assessing human health hazard. Off-topic references (e.g., studies that did not contain information relevant to human health) were excluded at either title/abstract screening (see Table C.3), or full-text screening (see Table C.4). Unacceptable references (e.g., studies that did not meet data quality metrics) were excluded at full-text screening (see Tables C.5 and C.6). Off-topic and unacceptable references are displayed next to the corresponding exclusion criteria.

Table C.3: Off-Topic References Excluded at Title/Abstract Screening for Human Health Hazard

Reference excluded (HERO ID) because the reference did NOT contain information needs[44] relevant to human health hazard									
33975	4949055	4948960	4947155	4705492	1201178	4949084	4948984	4948886	4946188
44187	4949056	4948961	4947156	4706833	1204953	4949085	4948985	4948887	4946189
404898	4949058	4948962	4947159	4738360	1249186	4949086	4948986	4948890	4946190
628230	4949060	4948963	4947160	4738993	1254062	4949087	4948988	4948891	4946193
628727	4949061	4948964	4947161	4742957	1314113	4949089	4948989	4948892	4946194
635083	4949063	4948965	4947175	4828940	1316100	4949090	4948990	4948893	4946210
744085	4949064	4948966	4947177	4828943	1321888	4949092	4948991	4948894	4946247
789593	4949065	4948967	4947178	4847997	1458307	4949094	4948992	4948895	4946257
789651	4949066	4948968	4947179	4853443	1496934	4949095	4948993	4948896	4946258
926985	4949067	4948969	4947182	4909646	1549118	4949096	4948994	4948898	4946259
992939	4949068	4948970	4947185	4940595	1580047	4949098	4948995	4948899	4946263

[44] 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.3: Off-Topic References Excluded at Title/Abstract Screening for Human Health Hazard									
1058389	4949070	4948971	4947187	4940694	1611582	4949099	4948996	4948900	4946320
1058433	4949071	4948972	4947189	4940855	1612753	4949100	4948997	4948902	4946322
1112905	4949072	4948974	4947194	4941419	1615034	4949102	4948998	4948904	4946324
1124442	4949074	4948975	4947200	4945941	1689217	4949103	4948999	4948905	4946329
1124901	4949075	4948977	4947201	4946008	1763085	4949104	4949000	4948906	4946359
1142139	4949076	4948978	4947202	4946061	1763087	4949105	4949001	4948909	4946360
1153582	4949078	4948979	4947203	4946132	1763125	4949106	4949002	4948911	4946361
1156301	4949080	4948980	4947204	4946147	1763137	4949108	4949003	4948912	4946374
1167387	4949081	4948981	4947223	4946178	1763157	4949109	4949004	4948913	4946375
1201159	4949082	4948982	4947224	4946179	1781960	4949110	4949005	4948914	4946376
1201176	4949083	4948983	4948885	4946180	1808388	4949111	4949006	4948915	4946380
3036899	4949156	4949040	4948950	4947131	1808755	4949112	4949007	4948916	4946387
3037885	4949157	4949042	4948951	4947132	1865871	4949113	4949009	4948918	4946408
3038973	4949158	4949044	4948952	4947135	1955931	4949116	4949010	4948919	4946410
3039406	4949159	4949045	4948953	4947136	1967450	4949117	4949011	4948920	4946411
3039791	4951048	4949046	4948954	4947137	1970619	4949118	4949012	4948921	4946419
3041527	4951050	4949047	4948955	4947138	2231679	4949119	4949013	4948922	4946423
3041622	4951055	4949049	4948956	4947140	2232056	4949120	4949015	4948923	4946506
3041638	4951170	4949051	4948958	4947141	2232422	4949121	4949016	4948925	4946513
3041935	4951176	4949052	4948959	4947154	2232425	4949122	4949017	4948926	4946538
3047394	4951181	4949053	4339757	4576534	2232427	4949123	4949018	4948927	4946547
3051635	4951206	4949054	4376725	4579583	2232444	4949126	4949020	4948928	4946614
3051709	4951208	3753956	4388064	4583202	2232562	4949128	4949021	4948930	4946615
3103598	4951228	3823035	4391261	4656492	2273142	4949129	4949022	4948931	4946617
3114932	4428638	3830342	4395587	4660346	2292715	4949130	4949023	4948932	4946619

Table C.3: Off-Topic References Excluded at Title/Abstract Screening for Human Health Hazard									
3115961	4428838	3830898	4398518	4704876	2302957	4949131	4949024	4948933	4946620
3119596	4433785	3846566	4399866	3577212	2530089	4949132	4949026	4948934	4946621
3225794	4436364	3847436	4400649	3577235	2563138	4949134	4949027	4948935	4946623
3374286	4436864	3874693	4404349	3590105	2692340	4949135	4949028	4948936	4947105
3402924	4438060	4146480	4408404	3619406	2745927	4949138	4949029	4948938	4947106
3445046	4438415	4148076	4420372	3625221	2824290	4949140	4949030	4948940	4947107
3476490	4425601	4148079	4420932	4275583	2875983	4949141	4949031	4948942	4947108
3477473	4426820	4168926	4420947	4276472	2883990	4949142	4949032	4948943	4947109
3491334	3559324	4173202	4421954	4423539	2887419	4949149	4949033	4948944	4947110
3539276	3562800	4222683	4948949	4947130	2892020	4949150	4949034	4948946	4947111
3009070	4949153	4949037	4948948	4947115	2978028	4949152	4949035	4948947	4947113
3036268	4949154	4949039							
Reference excluded (HERO ID) because the reference primarily contained *in silico* data									
N/A.									

Table C.4: Screening Questions and Off-Topic References Excluded at Full-text Screening for Human Health Hazard		
Question	**Off-topic if answer is:**	**References excluded (HERO ID)**
Does the reference contain information pertaining to a low- priority substance candidate?	No	1322754 1629162 1776453 1875316 2301122 2301139 3041082 4219489 4862648 4940454 4941418 4946053

Table C.4: Screening Questions and Off-Topic References Excluded at Full-text Screening for Human Health Hazard		
Question	**Off-topic if answer is:**	**References excluded (HERO ID)**
		4947114 4951209 61412 824457 1744616 1744618 3039593 4441664 4442235 4862648 4940287 4940288 4940320 4940383 4940385 4940387 4940395 4940392 4946053 4948456 4949088 4951173 4951178
What type of source is this reference?	Review article or book chapter that contains only citations to primary literature sources	1004739 3038211 4940386 4946377 628176 3036785
What kind of evidence does this reference primarily contain?	*In silico* studies that DO NOT contain experimental verification	N/A.

Table C.4: Screening Questions and Off-Topic References Excluded at Full-text Screening for Human Health Hazard		
Question	**Off-topic if answer is:**	**References excluded (HERO ID)**
The following question apply to HUMAN evidence only		
Does the reference report an exposure route that is or is presumed to be by an inhalation, oral, or dermal route?	No	N/A.
Does the reference report both test substance exposure(s) AND related health outcome(s)?	No	N/A.
If the reference reports an exposure to a chemical mixture, are measures of the test substance or related metabolite(s) reported independently of other chemicals? Note: If the paper does not pertain to mixtures, choose "Not Applicable".	No	4951213
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	4951261 4951218 4951185 1230541
Does the paper report a negative control that is a vehicle control or no treatment control?	No[45]	4951261
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	3036587

[45] 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.4: Screening Questions and Off-Topic References Excluded at Full-text Screening for Human Health Hazard		
Question	**Off-topic if answer is:**	**References excluded (HERO ID)**
Does the reference report an exposure to the test substance only (i.e. no mixtures with the exception of aqueous solutions and reasonable impurities and byproducts)?	No	N/A.
For genotoxicity studies only: Does the study use a positive control?	No	3036587

Table C.5: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Human Health Hazard – Animal		
Data Quality Metric	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 1: Test substance identity	• The test substance identity cannot be determined from the information provided (e.g., nomenclature was unclear and CASRN or structure were not reported). **OR** • For mixtures, the components and ratios were not characterized or did not include information that could result in a reasonable approximation of components.	N/A.
Metric 2: Negative and vehicle controls	A concurrent negative control group was not included or reported. **OR** The reported negative control group was not appropriate (e.g., age/weight of animals differed between control and treated groups).	N/A.
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).	1763148 3041958 4940388 4940524 4940510

Table C.5: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Human Health Hazard – Animal		
Data Quality Metric	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 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).	4940388 4940389 4941420 4946133
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).	4941420 1763148 4940389 4940388 3041958 4946133
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.).	1763148 2282271 4940388 4940389 4941420 4946133
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.	4940388 4940524 4941420 2282271 4442235 4940303 4940394

Table C.5: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Human Health Hazard – Animal		
Data Quality Metric	**Unacceptable if:**	**References excluded (HERO ID)**
		4946044 4940452

Table C.6: 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.	3039551
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.
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**	4940521 4940522 4940389 2282271

Table C.6: 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)**
	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).	
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).	4940451 4940388

C.2.2 Environmental Hazard

For the screening review of LPS candidate 1,1'-dimethyldiethylene glycol, EPA excluded a total of 547 references when assessing environmental hazard. Off-topic environmental hazard references excluded at title/abstract screening are listed in Table C.7, and those excluded at full-text screening are listed in Table C.8. References in Table C.9 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.7: Off-Topic References Excluded at Title/Abstract Screening for Environmental Hazard									
Reference excluded (HERO ID) because the reference did NOT contain information needs[46] relevant to environmental hazard									
44187	4440871	4949112	4948988	4946374	2892020	4738993	1744618	4949052	4948891
404898	4441664	4949113	4948989	4946375	2978028	4742957	1763125	4949053	4948892
635083	4442235	4949116	4948990	4946376	3009070	4828940	1763137	4949054	4948893
744085	4940392	4949117	4948991	4946377	3036268	4828943	1763148	4949055	4948894
789593	4940395	4949118	4948992	4946380	3036587	4847997	1763157	4949056	4948895
789651	4941420	4949119	4948993	4946387	3036785	4853443	1776453	4949058	4948896
824457	4944882	4949120	4948994	4946408	3036899	4862648	1808755	4949060	4948898
926985	4946008	4949121	4948995	4946419	3037885	4909646	2112816	4949061	4948899
1058389	4946016	4949122	4948996	4946513	3038211	4940595	2301122	4949063	4948900
1058433	4946044	4949123	4948997	4946538	3038973	4940694	2301139	4949064	4948902
1112905	4946053	4949126	4948998	4946547	3039406	4940855	2745927	4949065	4948904
1124442	4946054	4949128	4948999	4946614	3039551	4941418	3041082	4949066	4948905
1124901	4946055	4949129	4949001	4946615	3039791	4941419	3041527	4949067	4948906
1142139	4946135	4949130	4949002	4946617	3041935	4945941	3041622	4949068	4948909
1153582	4946142	4949132	4949003	4946619	3114932	4946061	3041638	4949070	4948911
1156301	4946194	4949134	4949004	4946620	3115961	4946132	3103598	4949071	4948912
1167387	4946244	4949135	4949005	4946623	3225794	4946133	3118622	4949072	4948913
1201159	4946247	4949138	4949006	4947105	3374286	4946147	4222683	4949074	4948914
1201176	4946261	4949140	4949007	4947107	3402924	4946178	4259576	4949075	4948915
1201178	4946314	4949141	4949009	4947108	3445046	4946179	4440869	4949076	4948916
1204953	4946316	4949142	4949010	4947109	3476490	4946180	4948954	4949078	4948918
1249186	4946333	4949149	4949011	4947110	3477473	4946188	4948955	4949080	4948919
1321888	4946334	4949150	4949012	4947111	3491334	4946189	4948956	4949081	4948920
1458307	4946361	4949152	4949013	4947113	3539276	4946190	4948958	4949082	4948921
1496934	4946362	4949153	4949015	4947114	3559324	4946191	4948959	4949083	4948922

[46] 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.7: Off-Topic References Excluded at Title/Abstract Screening for Environmental Hazard									
1549118	4946363	4949154	4949016	4947115	3562800	4946193	4948960	4949084	4948923
1611582	4946410	4949156	4949017	4947130	3577212	4946210	4948961	4949085	4948925
1612753	4946411	4949157	4949018	4947131	3577235	4946257	4948962	4949086	4948926
1615034	4946412	4949158	4949020	4947132	3590105	4946258	4948963	4949087	4948927
1689217	4946414	4949159	4949021	4947135	3619406	4946259	4948964	4949088	4948928
1781960	4946416	4951181	4949022	4947136	3625221	4946263	4948965	4949089	4948930
1808388	4946420	1763085	4949023	4947137	3753956	4946322	4948966	4949090	4948931
1865871	4946423	1763087	4949024	4947138	3830342	4946324	4948967	4949092	4948932
1875316	4946424	4946320	4949026	4947140	3830898	4946329	4948968	4949094	4948933
1955931	4946506	4949131	4949027	4947141	3846566	4946359	4948969	4949095	4948934
1967450	4946511	992939	4949028	4947155	3847436	4946360	4948970	4949096	4948935
1970619	4946541	3051635	4949029	4947156	3874693	4420932	4948971	4949098	4948936
2231679	4946621	3051709	4949030	4947159	4088550	4420947	4948972	4949099	4948938
2232056	4947224	4951048	4949031	4947160	4146480	4421954	4948974	4949100	4948940
2232422	4948456	2282271	4949032	4947161	4148076	4423539	4948975	4949102	4948942
2232425	4949000	33975	4949033	4947175	4148079	4425601	4948977	4949103	4948943
2232427	4951050	61412	4949034	4947177	4168926	4426820	4948978	4949104	4948944
2232444	4951055	628176	4949035	4947182	4173202	4428638	4948979	4949105	4948946
2232562	4951170	628230	4949037	4947185	4275583	4428838	4948980	4949106	4948947
2273142	4951173	628727	4949039	4947189	4276472	4433785	4948981	4949108	4948948
2292715	4951176	1004739	4949040	4947201	4339757	4436364	4948982	4949109	4948949
2302957	4951185	1230541	4949042	4947202	4376725	4436864	4948983	4949110	4948950
2563138	4951207	1254062	4949044	4947203	4388064	4438060	4948984	4949111	4948951
2692340	4951209	1314113	4949045	4947204	4391261	4438415	4948985	4579583	4948952
2824290	4951213	1316100	4949046	4948885	4395587	4576534	4948986	4583202	4948953
2875983	4951218	1322754	4949047	4948886	4398518	4404349	4705492	4660346	4420372
2883990	4951261	1580047	4949049	4948887	4399866	4408404	4706833	4704876	4400649
2887419	4738360	1629162	4949051	4948890					

Table C.7: Off-Topic References Excluded at Title/Abstract Screening for Environmental Hazard
Reference excluded (HERO ID) because the reference did NOT present quantitative environmental hazard data
N/A.

Table C.8: 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	1580138 4731313 4851358 4951178 1744616 4940286 4951206 4951228 4940436 4947106 4951208
What type of source is this reference?	Review article or book chapter that contains only citations to primary literature sources	4219489
Is quantitative environmental hazard data presented?	No	N/A.
Is this primarily a modeling/simulation study? [Note: select "No" if experimental verification was included in the study]	Yes	N/A.
Is environmental hazard data presented for standard or non-standard aquatic or terrestrial species (fish, invertebrates, microorganisms, non-mammalian terrestrial species)?	No	N/A.
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	7504 4940435

Table C.8: Screening Questions and Off-Topic References Excluded at Full-text Screening for Environmental Hazard		
Question	**Off-topic if answer is:**	**References excluded (HERO ID)**
		4940366 4940397
Does the reference include endpoints in the information needs?	No	N/A.

Table C.9: 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.	4951174 4951208
Metric 3: Experimental System	The experimental system (e.g., static, semi-static, or flow-through regime) was not described.	4940436 4940440 4951174 4940388 3041958
Metric 4: Reporting of Concentrations	Test concentrations were not reported.	4951174 4951208
Metric 5: Exposure Duration	The duration of exposure was not reported. **OR** The reported exposure duration was not suited to the study type and/or outcome(s) of interest (e.g., study intended to assess effects on reproduction did not expose organisms for an acceptable period of time prior to mating).	4951208 4951174
Metric 6: Test Organism Characteristics	The test species was not reported. **OR**	N/A.

Table C.9: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Environmental Hazard		
Question	**Unacceptable if:**	**References excluded (HERO ID)**
	The test species, life stage, or age was not appropriate for the outcome(s) of interest.	
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.	4940388 3041958

C.3 Fate

For the screening review of LPS candidate 1,1'-dimethyldiethylene glycol, EPA excluded a total of 453 references when assessing environmental fate. Off-topic fate references excluded at title/abstract screening are listed in Table C.10, and those excluded at full-text screening are listed in Table C.11. References in Table C.12 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.10: Off-Topic References Excluded at Initial Screening for Fate									
Reference excluded (HERO ID) because the reference did NOT contain information needs[47] relevant to environmental fate									
44187	4949033	4948959	4946621	4146480	2232444	4949089	4949005	4948895	4847997
404898	4949034	4948960	4946623	4148076	2232562	4949090	4949006	4948896	4853443
635083	4949035	4948961	4947105	4148079	2273142	4949092	4949007	4948898	4862648
744085	4949037	4948962	4947107	4168926	2292715	4949094	4949009	4948899	4909646
789593	4949039	4948963	4947108	4173202	2302957	4949095	4949010	4948900	4940595
789651	4949040	4948964	4947109	4275583	2563138	4949096	4949011	4948902	4940694
824457	4949042	4948965	4947110	4276472	2692340	4949098	4949012	4948904	4940855
926985	4949044	4948966	4947111	4339757	2824290	4949099	4949013	4948905	4941418
992939	4949045	4948967	4947113	4376725	2875983	4949100	4949015	4948906	4941419
1058389	4949046	4948968	4947114	4388064	2883990	4949102	4949016	4948909	4941420

[47] 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.10: Off-Topic References Excluded at Initial Screening for Fate									
1058433	4949047	4948969	4947115	4391261	2887419	4949103	4949017	4948911	4945941
1112905	4949049	4948970	4947130	4395587	2892020	4949104	4949018	4948912	4946061
1124442	4949051	4948971	4947131	4398518	2978028	4949105	4949020	4948913	4946132
1124901	4949052	4948972	4947132	4399866	3009070	4949106	4949021	4948914	4946133
1142139	4949053	4948974	4947135	4400649	3036268	4949108	4949022	4948915	4946147
1153582	4949054	4948975	4947136	4404349	3036587	4949109	4949023	4948916	4946178
1156301	4949055	4948977	4947137	4408404	3036785	4949110	4949024	4948918	4946179
1167387	4949056	4948978	4947138	4420372	3036899	4949111	4949026	4948919	4946180
1201159	4949058	4948979	4947140	4420932	3037885	4949112	4949027	4948920	4946188
1201176	4949060	4948980	4947141	4420947	3038211	4949113	4949028	4948921	4946189
1201178	4949061	4948981	4947155	4421954	3038973	4949116	4949029	4948922	4946190
1204953	4949063	4948982	4947156	4423539	3039406	4949117	4949030	4948923	4946191
1249186	4949064	4948983	4947159	4425601	3039551	4949118	4949031	4948925	4946193
1321888	4949065	4948984	4947160	4426820	3039791	4949119	4949032	4948926	4946194
1458307	4949066	4948985	4947161	4428638	3041935	4949120	4946380	4948927	4946210
1496934	4949067	4948986	4947175	4428838	3114932	4949121	4946387	4948928	4946247
1549118	4949068	4948988	4947177	4433785	3115961	4949122	4946408	4948930	4946257
1611582	4949070	4948989	4947182	4436364	3225794	4949123	4946410	4948931	4946258
1612753	4949071	4948990	4947185	4436864	3374286	4949126	4946419	4948932	4946259
1615034	4949072	4948991	4947189	4438060	3402924	4949128	4946506	4948933	4946263
1689217	4949074	4948992	4947201	4438415	3445046	4949129	4946513	4948934	4946322
1781960	4949075	4948993	4947202	4576534	3476490	4949130	4946538	4948935	4946324
1808388	4949076	4948994	4947203	4579583	3477473	4949132	4946547	4948936	4946329
1865871	4949078	4948995	4947204	4583202	3491334	4949134	4946614	4948938	4946359
1875316	4949080	4948996	4947224	4660346	3539276	4949135	4946615	4948940	4946360
1955931	4949081	4948997	4948885	4704876	3559324	4949138	4946617	4948942	4946361
1967450	4949082	4948998	4948886	4705492	3562800	4949140	4946619	4948943	4946374
1970619	4949083	4948999	4948887	4706833	3577212	4949141	4946620	4948944	4946375
2231679	4949084	4949000	4948890	4738360	3577235	4949142	4948952	4948946	4946376
2232056	4949085	4949001	4948891	4738993	3590105	4949149	4948953	4948947	4946377
2232422	4949086	4949002	4948892	4742957	3619406	4949150	4948954	4948948	4949157
2232425	4949087	4949003	4948893	4828940	3625221	4949152	4948955	4948949	4949158
2232427	4949088	4949004	4948894	4828943	3753956	4949153	4948956	4948950	4949159
3830898	4949156	3847436	3874693	4088550	3830342	4949154	4948958	4948951	4951181

Table C.10: Off-Topic References Excluded at Initial Screening for Fate									
3846566									
Reference excluded (HERO ID) because the reference did NOT present quantitative environmental fate data									
N/A.									

Table C.11: 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	4940397 4940399 4949131 1763087 4940401
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.12: 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**	4940366 4940402 4940404

Table C.12: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Fate		
Data quality metric	**Unacceptable if:**	**References excluded (HERO ID)**
	The vehicle used in the study was likely to unduly influence the study results.	
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.	4940404 4940430
Metric 4: Test method suitability	The test method was not reported or not suitable for the test substance. **OR** The test concentrations were not reported. **OR** The reported test concentrations were not measured, and the nominal concentrations reported greatly exceeded the substances water solubility, which would greatly inhibit meaningful interpretation of the outcomes.	4940402 4940404
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).	4940366 4940402 4940404
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.

Table C.12: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Fate		
Data quality metric	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 7: Test organism-degradation	The test organism, species, or inoculum source were not reported, preventing meaningful interpretation of the study results.	4940402 4940430
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.	1763085 4940402 4940404 4940388 4940389
Metric 10: Data reporting	Insufficient data were reported to evaluate the outcome of interest or to reasonably infer an outcome of interest. **OR** The analytical method used was not suitable for detection or quantification of the test substance. **OR** Data indicate that disappearance or transformation of the parent compound was likely due to some other process.	N/A.
Metric 11: Confounding Variables	There were sources of variability and uncertainty in the measurements and statistical techniques or between study groups.	4940402 4940404 4940430
Metric 12: Verification or plausibility of results	Reported value was completely inconsistent with reference substance data, related physical chemical properties, or otherwise implausible, suggesting that a serious study deficiency exists (identified or not).	1763085 4940366 4940402 4940404