Supporting Information for Low-Priority Substance Propanol, [2-(2-Butoxymethylethoxy)Methylethoxy]- (CASRN 55934-93-5) (Tripropylene Glycol n-Butyl Ether)

Final Designation

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Contents

Tables

1. Introduction

The Lautenberg amendments to the Toxic Substances Control Act (TSCA) require EPA to designate chemical substances as either High-Priority Substances for risk evaluation, or Low-Priority Substances for which risk evaluations are not warranted at this time (section 6(b)(1)(B) and implementing regulations (40 CFR 702.3)). A high-priority substance is defined as a chemical substance that the Administrator concludes, without consideration of costs or other non-risk factors, may present an unreasonable risk of injury to health or the environment because of a potential hazard and a potential route of exposure under the conditions of use, including an unreasonable risk to potentially exposed or susceptible subpopulations identified as relevant by the Administrator. If the Administrator concludes, based on information sufficient to establish, without consideration of costs or other non-risk factors, that the high-priority standard is not met, then the substance must be designated as a low-priority substance. Propanol, [2-(2-butoxymethylethoxy)methylethoxy]-, referenced as tripropylene glycol n-butyl ether 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 does not meet the statutory criteria for a high-priority substance and that a risk evaluation is not warranted at the time. As explained in the preamble to the Prioritization Rule, "low-priority substance designations give the public notice of chemical substances for which the hazard and/or exposure potential is anticipated to be low or nonexistent and provides some insight into which chemical substances are likely not to need additional evaluation and risk management under TSCA." 82 FR 33753 at 33755. EPA is not precluded from later revising the designation based on reasonably available information, if warranted. 40 CFR 702.13; 702.15.

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

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

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

The screening review is not a risk evaluation, but rather a review of reasonably available information on the chemical substance that relates to the specific criteria and considerations in TSCA section 6(b)(1)(A) and 40 CFR 702.9. This paper documents the results of the screening review which supports the final designation of tripropylene glycol n-butyl 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.

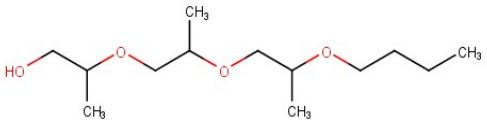
- *Appendix B (Hazard Characterization):* This appendix contains information on each of the studies used to support the hazard evaluation of the chemical substance.

- *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.

- *Appendix D (Summary of Public Comments):* This appendix includes sources of information for the chemical substance that the public recommended to EPA during a 90-day comment period.

2. Background on Tripropylene Glycol n-Butyl Ether

Table 1 below provides the CAS number, synonyms, and other information on tripropylene glycol n-butyl ether.

Table 1: Tripropylene Glycol n-Butyl Ether at a Glance	
Chemical Name	Tripropylene Glycol n-Butyl Ether
CASRN	55934-93-5
Synonyms	Tripropylene glycol butyl ether; Tripropylene glycol monobutyl ether; (2-(2-Butoxymethylethoxy)methylethoxy) propanol; ((Butoxymethylethoxy)methylethoxy)propan-1-ol; 1-[(2-Butoxy-1-methylethoxy)-1-methylethoxy]-2- propanol; PPG-3 butyl ether
Trade Name(s)	DOWANOL TPnB Glycol Ether; TPnB
Molecular Formula	$C_{13}H_{28}O_4$
Representative Structure	

Tripropylene glycol n-butyl ether (TPnB) is a P-series glycol ether, meaning that it is made from propylene oxide. Glycol ethers are organic chemical compounds that contain both an alcohol functional group (R-OH) and an ether functional group, which is an oxygen atom connected to two alkyl groups (R-O-R'). TPnB is a linear molecule that can be composed of three isomeric propylene oxide groups linked together through ether groups, terminating in a n-butyl carbon chain on one end and an alcohol on the other. Shorter chain ethers and esters, such as TPnB, are liquids capable of dissolving other substances and typically function as solvents. TPnB is a colorless to light yellow hydrophobic liquid with a high boiling point and low volatility. These properties make TPnB a useful solvent, coalescing agent, and film-forming agent 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 tripropylene glycol n-butyl ether. 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 TPnB

Source/ Model	Data Type	Endpoint	Endpoint value	Notes
Sigma Aldrich 2019	Experimental	Physical state at room temp (based on melting point)	Liquid (-75°C)	
Staples and Davis 2002	Experimental	Molecular weight	248 g/mol	
EPISuite v.4.11[4]	Calculated	Molecular weight	248.4 g/mol	
Lyman 1990	Calculated	Molar volume	336.4 cm^3/mol	
Staples and Davies 2002	Experimental	Water solubility	25,000 mg/L	
Reported to the ECHA database, 2018	Experimental	Water solubility	40,200 mg/L at 20°C at pH 7; 46,000 mg/L (4.6 wt%) at 20°C at pH 7; 25,000 mg/L at 20°C at pH 7	
EPISuite v.4.11	Estimated	Water solubility	8,187 mol/L(from Log K_{ow}); 95,000 mg/L (fragment method)	
Staples and Davis 2002	Experimental	Water solubility	0.101 mol/L	
Reported to the ECHA database, 2019	Experimental	Water solubility	0.162 mol/L; 0.185 mol/L; 0.101 mol/L	

[4] EPI Suite Physical Property Inputs – Melting Point= -75 deg C; Log P = 1.896; Water Solubility = 25000 mg/L; Henry's Law Constant = 4.05E-08 atm-m3/mole; SMILES: OC(C)COC(C)COC(C)COCCCC

Table 2: Physical-Chemical Properties for TPnB				
Source/ Model	**Data Type**	**Endpoint**	**Endpoint value**	**Notes**
Staples and Davis 2002	Experimental	Log K_{ow}	1.9	ECHA reports a calculated Log K_{ow} that is identical to the measured value presented in Staples and Davis 2002
EPISuite v.4.11	Estimated	Log K_{ow}	1.3	
EPISuite v.4.11	Estimated	Log K_{oa}	7.68	
EPISuite v.4.11	Estimated	Log K_{oc}	1 (MCI); 1.29 (K_{ow})	
Staples and Davis 2002	Experimental	Vapor pressure	3.08×10^{-3} mm Hg (0.41 Pa) at 25°C	
Reported to the ECHA database 2019	Experimental	Vapor pressure	1.5×10^{-3} mm Hg (0.2 Pa at 20°C); 2.3×10^{-3} mm Hg (0.3 Pa at 25°C)	
EPISuite v.4.11	Estimated	Vapor pressure	1.08×10^{-4} mm Hg	
EPISuite v.4.11	Estimated	Henry's Law constant	3E-8 atm-m^3/mole	
Staples and Davis 2002	Experimental	Henry's Law constant	4.05E-8 atm-m^3/mole	Calculated from experimental vapor pressure and water solubility
EPISuite v.4.11	Estimated	Volatilization	960 days (river) 1.05×10^4 days (lake)	
EPISuite v.4.11	Estimated	Photolysis (Indirect)	1.80 hours ($T_{1/2}$)	• OH rate constant 7.15 E-11 cm^3/molecules-sec (12 hour day; 1.5E6 OH/cm^3) • No ozone reaction estimation
EPISuite v.4.11	Estimated	Hydrolysis	Rate constants cannot be estimated	Not hydrolyzable
EPISuite v.4.11	Estimated	Biodegradation potential	Ready prediction: No	
EPISuite v.4.11	Estimated	Wastewater treatment plant removal	94% Total Removal (93% biodegradation, 0.40% sludge, 0.22% air)	Input parameters: BIOP = 4, BioA = 1 and BioS = 1 based on 72% degraded after 10d window and 107% after 28 days in a 301F test
EPISuite v.4.11	Estimated	BAF	6.22	
EPISuite v.4.11	Estimated	BCF	8.22	Based on regression equation

EPA's Sustainable Futures/P2 Framework Manual[5] was used to interpret the physical-chemical properties provided in Table 2. Based on its reported physical form and measured melting point, tripropylene glycol n-butyl ether is a liquid under ambient conditions. Liquids have the potential for exposure via direct dermal contact with the substance, ingestion, or by inhalation of aerosols if they are generated. Exposure through direct dermal contact with this substance is expected to result in poor to moderate dermal absorption based on its molecular weight, water solubility and log K_{ow}. Based on its measured vapor pressure (Staples and Davis, 2002), tripropylene glycol n-butyl ether is expected to volatilize at ambient temperatures. As a result, exposure to tripropylene glycol n-butyl ether is possible through inhalation of vapors or aerosols if they are generated. Based on measured solubility data (Staples and Davis, 2002), tripropylene glycol n-butyl ether 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 tripropylene glycol n-butyl ether is present in dilute form. The Henry's Law constant (Staples and Davis, 2002) for this compound indicates that volatilization from water and aqueous solutions is expected to be minimal and therefore exposure through breathing vapor from a dilute form is expected to be minimal. Based on its estimated log K_{ow} (EPI Suite, 2019), tripropylene glycol n-butyl ether is unlikely to cross lipid membranes. Absorption and sequestration in fatty tissues is therefore unlikely, as reflected in the estimated bioconcentration factor (BCF) and bioaccumulation (BAF) values for this compound (EPI Suite, 2019). The estimated log K_{oc} (EPI Suite, 2019) indicates tripropylene glycol n-butyl ether is highly mobile in soils, increasing its potential for leaching into and transport in 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 expected to be moderated based on the log K_{ow} (EPI Suite, 2019). Concern for presence in drinking water is reduced in part by tripropylene glycol n-butyl ether's expected low persistence. Experimental data indicate tripropylene glycol n-butyl ether is readily biodegradable (Dow Chemical, 1998; Reported to the ECHA database, 1998) meaning that it has the potential to break down in the environment.

3.1 References

European Chemicals Agency (ECHA). (2019). [(butoxymethylethoxy)methylethoxy]propan-1-ol. Retrieved from https://Echa.europea.eu/substance-information/-/substanceinfo/100.054.446

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

Sigma Aldrich (2019). Tri(propylene glycol) butyl ether, mixture of isomers. Retrieved from https://www.sigmaaldrich.com/catalog/product/aldrich/484229?lang=en&region=US

Staples, CA; Davis, JW. (2002). An examination of the physical properties, fate, ecotoxicity and potential environmental risks for a series of propylene glycol ethers. Chemosphere, Oct;49(1):61-73.

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

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

4. Relevant Assessment History

EPA assessed the toxicological profile of tripropylene glycol n-butyl ether 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[6] is a continuously updated list of chemicals that meet low-concern Safer Choice criteria.[7]

Internationally, EPA identified one assessment by the German Environmental Agency (UBA), which designated tripropylene glycol n-butyl ether as "low hazard to waters" in August 2017 based on an assessment of ecotoxicity and environmental fate.[8]

[6] https://www.epa.gov/saferchoice/safer-ingredients
[7] https://www.epa.gov/sites/production/files/2013-12/documents/dfe_master_criteria_safer_ingredients_v2_1.pdf
[8] https://webrigoletto.uba.de/rigoletto/public/searchDetail.do?kennummer=7169

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 tripropylene glycol n-butyl ether (Appendix A) to inform which uses would be determined conditions of use.[9] One source of information that EPA used to understand 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. 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, tripropylene glycol n-butyl ether is imported. It is used in processing (incorporation into formulation, mixture or reaction) for other basic organic chemicals. It has industrial uses (non-incorporative activities for coatings, construction, mining chemicals, oil and gas drilling, and wholesale and retail trade). Consumer uses include cleaning and furnishing care products, air care products, anti-freeze and deicing products, and inks, toners, and colorant products. Based on the known manufacturing, processing, and uses of this chemical substance, EPA assumes distribution in commerce. According to CDR, three facilities reported that the chemical was not recycled, and one facility reported this information as confidential business information (CBI). No information on disposal is found in CDR or through EPA's Toxics Release Inventory (TRI) Program[10] because tripropylene glycol n-butyl ether is not a TRI-reportable chemical. Although reasonably available information did not specify additional types of disposal, for purposes of this 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 identify additional occupational[11] and consumer uses. This research improved the Agency's understanding of the conditions of use for tripropylene glycol n-butyl ether. Although EPA identified uses of tripropylene glycol n-butyl ether 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 tripropylene glycol n-butyl ether considered for chemical substance prioritization, per TSCA section 3(4). Table 3 reflects the TSCA uses determined as conditions of use listed in Table A.3 (Appendix A).

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

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

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

Table 3: Conditions of Use for Tripropylene Glycol n-Butyl Ether			
Life Cycle Stage	**Category**	**Subcategory of Use**	**Source**
Manufacturing	Import	Import	EPA (2017b)
Processing	Processing- incorporation into formulation, mixture or reaction	Solvents: all other basic organic chemical	EPA (2017b)
	Processing- incorporation into formulation, mixture or reaction	Coatings, paint manufacturing	Reported to the ECHA database (2018), CPCat (2019)
	Recycling	Recycling	EPA (2017b)[12]
Distribution	Distribution	Distribution	EPA (2017b)
Industrial	Use—non-incorporative activities	Communication equipment manufacturing, electrical manufacturing, fabricated metal product manufacturing, furniture manufacturing, wood manufacturing, construction, mining chemicals, oil and gas drilling, wholesale and retail trade	Reported to the ECHA database (2018), CPCat (2019)
		Processing aids, not otherwise listed	EPA (2017b)
		Plasticizers- wholesale and retail trade	
Commercial uses	Cleaning and furniture care products	Metal cleaner/ polish	CLR Brands (2018d)
Industrial/commercial		Metal working fluids	Reported to the ECHA database (2018)
Commercial/consumer	Cleaning and furniture care products	Bath cleaner, descalers, degreaser, kitchen cleaner, mold and mildew stain remover	CLR Brands (2018a); CLR Brands (2018b); CLR Brands (2018f); CPCat (2019), CLR Brands (2018c), CLR Brands (2018g)
Consumer	Air care products	Air care products	Reported to the ECHA database (2018)
	Cleaning and furniture care products	Hardwood floor finish, multi-surface cleaner	DeLima Associates (2018b), CLR Brands (2018e), EPA (2017b)
	Adhesives and sealants		Reported to the ECHA database (2018)

[12] In the 2016 CDR, three facilities reported that the chemical was not recycled, and one facility reported this information as CBI.

Table 3: Conditions of Use for Tripropylene Glycol n-Butyl Ether			
Life Cycle Stage	**Category**	**Subcategory of Use**	**Source**
	Anti-freeze and de-icing products		Reported to the ECHA database (2018)
	Inks, toners, and colorant products	Inks and toners	
	Fabric, textile, and leather products not covered elsewhere	Leather treatment products	
Disposal	Releases to air, wastewater, solid and liquid wastes.	Releases to air, wastewater, solid and liquid wastes.	Though not explicitly identified, releases from disposal were assumed to be reasonably foreseen[13]

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

6. Hazard Characterization

EPA reviewed primary literature and other data sources to identify reasonably available information. This literature review approach[14] is tailored to capture the reasonably available information associated with low-hazard chemicals. EPA also used this process to verify the reasonably available information for reliability, completeness, and consistency. EPA reviewed the reasonably available information to identify relevant, quality studies to evaluate the hazard potential for tripropylene glycol n-butyl ether against the endpoints listed below. EPA's New Chemicals Program has used these endpoints for decades to evaluate chemical substances under TSCA[15] and EPA toxicologists rely on these endpoints as key indicators of potential human health and environmental effects. These endpoints also align with internationally accepted hazard characterization criteria, such as the Globally Harmonized System of Classification and Labelling of Chemicals[16] as noted above in Section 4 and form the basis of the comparative hazard assessment of chemicals.

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

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

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

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

Human Health				
Acute Mammalian Toxicity[17]	**Very High**	**High**	**Moderate**	**Low**
Oral LD50 (mg/kg)	≤ 50	> 50 – 300	> 300 - 2000	> 2000
Dermal LD50 (mg/kg)	≤ 200	> 200 – 1000	> 1000 - 2000	> 2000
Inhalation LC50 (vapor/gas) (mg/L)	≤ 2	> 2 – 10	> 10 - 20	> 20
Inhalation LC50 (dust/mist/fume) (mg/L)	≤ 0.5	> 0.5 - 1.0	> 1.0 - 5	> 5

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

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

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

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

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

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

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

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

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

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

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

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

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

Table 4: Low concern Criteria for Human Health and Environmental Fate and Effects			
Environmental Fate and Effects			
Acute Aquatic Toxicity Value (L/E/IC50)[25]	**Chronic Aquatic Toxicity Value (L/E/IC50)[25]**	**Persistence (Measured in terms of level of biodegradation)[26]**	**Bioaccumulation Potential[27]**
May be low concern if ≤10 ppm…	…and ≤1 ppm…	…and the chemical meets the 10-day window as measured in a ready biodegradation test…	…and BCF/BAF < 1000.
Low concern if >10 ppm and <100 ppm…	…and >1 ppm and <10 ppm…	…and the chemical reaches the pass level within 28 days as measured in a ready biodegradation test	
Low concern if ≥100 ppm…	…and ≥ 10 ppm…	… and the chemical has a half-life < 60 days…	

6.1 Human Health Hazard

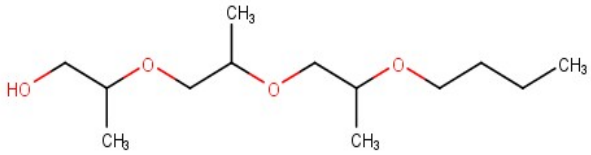
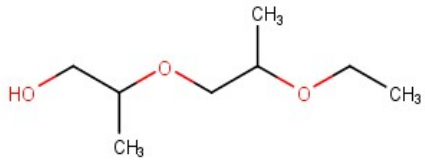
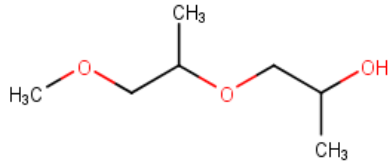
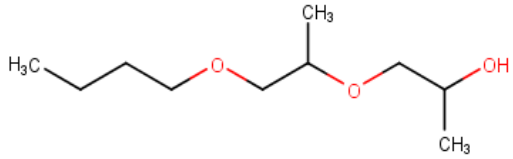
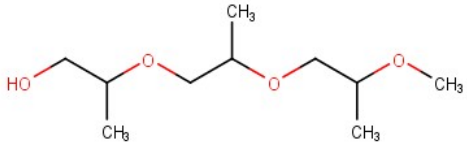
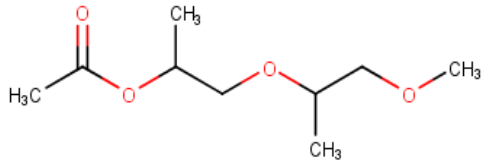
Below is a summary of the reasonably available information that EPA included in the hazard evaluation of tripropylene glycol n-butyl ether. In many cases, EPA used analogous chemicals to make findings for a given endpoint. Where this is the case, use of the analog is explained. If the chemical studied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

Tripropylene glycol n-butyl ether is a propylene glycol ether composed of three 1-methylethoxy repeating units with an n-butyl ether substitution on one of the terminal alcohols. EPA used best professional judgement to select analogs 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. All analogs used to inform EPA's understanding of this chemical are either di- or tri-propylene glycol ethers or ether acetates that vary by the length of the aliphatic ether chain length (methyl, ethyl or butyl). All of the glycol ethers are expected to metabolize via similar pathways *in vivo*. The glycol ether acetate is expected to rapidly hydrolyze *in vivo* to the corresponding propylene glycol ether. As noted in the table, four of the analogs are named as isomeric mixtures that may contain either the 1-methylethyl or 2-methylethyl substitution patterns in each propylene glycol unit. For ethers of dipropylene glycol and tripropylene glycol, the structural differences among the individual possible isomers are not expected to result in significant differences in the properties, persistence or hazards of these chemicals. Based on these factors, the environmental and toxicological effects of these analogs are expected to be very similar to those of tripropylene glycol n-butyl ether.

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

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

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

Table 5: Tripropylene Glycol n-Butyl Ether and Analog Structures		
CASRN	**Name**	**Structure**
55934-93-5	Tripropylene glycol n-butyl ether (isomeric mixture)	
30025-38-8	Dipropylene glycol monoethyl ether (isomeric mixture)	 Representative structure
34590-94-8	Dipropylene glycol, methyl ether (isomeric mixture)	 Representative structure
29911-28-2	Dipropylene glycol monobutyl ether	
25498-49-1	Tripropylene glycol monomethyl ether (isomeric mixture)	 Representative structure
88917-22-0	Dipropylene glycol methyl ether acetate (isomeric mixture)	

Dipropylene glycol, ethyl ether (CASRN 15764-24-6) and tripropylene glycol methyl ether (CASRN 20324-33-8) were also included in analog data searches; relevant, quality studies[28] were only identified for the CASRNs listed in Table 5.

6.1.1 Absorption, Distribution, Metabolism, and Excretion

To review absorption, distribution, metabolism and excretion (ADME) endpoints without adequate quality[28] experimental data, EPA used widely accepted new approach methodologies (NAMs), such as modeling and estimation tools often based on physical-chemical properties, which provided information sufficient to fill these endpoints.

Absorption

Based on tripropylene glycol n-butyl ether's molecular weight and water solubility (Table 2), tripropylene glycol n-butyl ether is expected to be absorbed through the gastrointestinal tract if oral ingestion occurs. If inhalation exposure occurs, it is also expected to be absorbed through the lungs based on the same physical-chemical properties. These properties, along with the log k_{ow} (Table 2), indicate poor to moderate skin absorption is expected if dermal exposure occurs.

Distribution

Because tripropylene glycol n-butyl ether is water soluble (Section 3), it is expected to be widely distributed throughout the body to various tissues including the liver, kidney and skin after an oral exposure. However, based on its log K_{ow} (Section 3), absorption and sequestration in fatty tissues is unlikely.

Metabolism

Experimental data determined to be of adequate quality[29] on tripropylene glycol n-butyl ether metabolite formation were not reasonably available for the assessment of metabolism. The Quantitative Structure-Activity Relationship (QSAR) toolbox[30] was used to run the rat liver S9 metabolism simulator, the skin metabolism simulator, and the *in vivo* rat metabolism simulator. The QSAR toolbox was used to identify putative tripropylene glycol n-butyl ether metabolites. The predicted metabolites from the skin metabolism simulator included propionic acid, propanal, butanal and 1-butanol. Additional metabolites of tripropylene glycol n-butyl ether identified by one or more of the metabolism simulators included derivative primary and secondary alcohols, carboxylic acids, aldehydes, ketones and secondary diols.

Excretion

Based on the molecular weight and water solubility (Section 3) of tripropylene glycol n-butyl ether, after metabolism tripropylene glycol n-butyl ether is expected to be excreted primarily in urine and exhaled air.

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[28] Data quality is discussed in the document "Approach Document for Screening Hazard Information for Low-Priority Substances Under TSCA."

[29] 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

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

6.1.2 Acute Toxicity

EPA assessed the mammalian toxicity potential from acute exposure by tripropylene glycol n-butyl ether using experimental evidence from oral, dermal, and inhalation exposures.

Two OECD Guideline 401 studies of rats exposed to a single oral dose of tripropylene glycol n-butyl ether were available (Reported to the ECHA database, 1988b, c). One study reported no mortalities, resulting in an LD_{50} greater than 2000 mg/kg (Reported to the ECHA database, 1988b). The second study reported an LD_{50} of 2800 mg/kg (Reported to the ECHA database, 1988c). An OECD Guideline 423 study exposed rats to a single dose (2000 mg/kg) of tripropylene glycol n-butyl ether by oral gavage (Reported to the ECHA database, 2001b). There was one mortality (out of twelve animals), resulting in an LD_{50} of greater than 2000 mg/kg. These studies provide sufficient information to indicate low concern for acute, oral toxicity with expected LD_{50}s above the low-concern benchmark of 2000 mg/kg.

Rats exposed to tripropylene glycol n-butyl ether dermally reported no mortalities at the single dose tested (2000 mg/kg), resulting in an LD_{50} greater than 2000 mg/kg (Reported to the ECHA database, 1988a). This study provides sufficient information to indicate low concern for acute, dermal toxicity with an expected LD_{50} above the low-concern benchmark of 2000 mg/kg.

EPA also assessed the mammalian toxicity potential from acute exposure to tripropylene glycol n-butyl ether using an inhalation exposure study from an analog, dipropylene glycol methyl ether acetate (DPMA). A study on rats exposed via inhalation to 5.7 mg/L (734 ppm) of DPMA vapor for four hours and observed for two weeks reported no mortalities (OECD, 2003; Reported to the ECHA database, 1982). This concentration exceeds the expected air saturation concentration of 135 ppm, indicating no effects at complete air saturation (OECD, 2003). These results provide sufficient information to indicate low concern for acute, inhalation toxicity based on no effects at air saturation.

6.1.3 Repeated Dose Toxicity

EPA assessed the potential for toxicity from repeated exposures by tripropylene glycol n-butyl ether using experimental data and read-across from analogs.

A study on rats exposed to tripropylene glycol n-butyl ether via oral gavage for 28 days resulted in a no observed adverse effect level (NOAEL) of 100 mg/kg-day and a lowest observed adverse effect level (LOAEL) of 350 mg/kg-day based on increases in both absolute and relative liver weights, though quantitative data were not available from the study to determine the biological significance of these increases (Reported to the ECHA database, 1990c). Another study on rats exposed to tripropylene glycol n-butyl ether orally for 13 weeks reported a NOAEL of 350 mg/kg-day and a LOAEL of 1000 mg/kg-day based on increased hepatocyte size, altered cytoplasm staining in the liver, and increases in absolute and relative liver and kidney weights. EPA considered these effects adaptive and reversible because the effects were not seen following a 4-week recovery period in a group exposed to 1000 mg/kg-day (Reported to the ECHA database, 1991). Based on the results of the 13-week study, the experimental results provide sufficient information to indicate low concern for toxicity resulting from repeated oral exposures by exceeding the low-concern benchmark of 100 mg/kg-day for 90-day studies or 300 mg/kg-day for 30-day studies.

Two 90-day dermal studies in rabbits exposed to dipropylene glycol, methyl ether reported an NOAEL of 4750 mg/kg-day (Dow Chemical, 2000a) and an LOAEL of 9500 mg/kg-day (Dow Chemical, 2000b; Rowe et al., 1954). A dermal study in rats exposed to dipropylene glycol, methyl ether for 28 days reported a NOAEL of 714 mg/kg-day (Fairhurst et al., 1989). Another study on rats exposed dermally to dipropylene glycol monobutyl ether for 13-weeks reported a NOAEL of 91 mg/kg-day and LOAEL of 273 mg/kg-day based on decreased body weight in males and increased white blood cell count in both sexes (OECD, 2003). However, the body weight changes only occurred in males, the increased white blood cell count was likely due to inflammation, and both effects were considered mild in nature. EPA also considered a study on rabbits dermally exposed to another analog, tripropylene glycol monomethyl ether, for 90 days. The study reported a NOAEL of 960 mg/kg-day and a LOAEL of 2900 mg/kg-day based on decreased body weight and increased kidney weight (Dow Chemical, 2000c; Rowe et al., 1954). The weight of the scientific evidence across the dermal data from multiple analogs indicates either no adverse effects or effects at doses that exceed the low-concern benchmark of 200 mg/kg-day for 90-day studies or 600 mg/kg-day for approximately 30-day studies. Therefore, these results provide sufficient information to indicate that tripropylene glycol n-butyl ether has low concern for dermal repeated dose toxicity.

A 13-week inhalation study in rats and rabbits exposed to dipropylene glycol, methyl ether reported no adverse effects at the highest tested concentration (1.212 mg/L), resulting in a NOAEC of 1.212 mg/L (Landry and Yano, 1984). This result provides sufficient information to indicate low concern for repeated inhalation toxicity by exceeding the low-concern benchmark of 1 mg/L for vapor inhalation exposures.

6.1.4 Reproductive and Developmental Toxicity

EPA used read across from closely-related analogs to evaluate tripropylene glycol n-butyl ether's potential to induce reproductive and developmental toxicity.

A one-generation reproductive study in rats exposed to dipropylene glycol monobutyl ether by oral gavage reported a reproductive NOAEL of 1000 mg/kg-day (Reported to the ECHA database, 1994). There were no adverse effects on reproductive parameters in parents and developmental effects in offspring, including physical and behavioral outcomes (i.e. reflexology). These results provide sufficient information to indicate low concern for reproductive toxicity by exceeding the low-concern oral benchmark of 250 mg/kg-day.

In a prenatal study of rats exposed dermally to dipropylene glycol n-butyl ether from gestation days (GD) 6-15, no adverse maternal toxicity or fetal toxicity was observed at the highest dose of 910 mg/kg-day (OECD, 2003). These results provide sufficient information to indicate low concern for developmental toxicity by exceeding the low-concern dermal benchmark of 500 mg/kg-day.

A developmental inhalation study in rats exposed to tripropylene glycol monomethyl ether aerosol from GD 6-15 reported a no observed adverse effect concentration (NOAEC) of 8.9 mg/L (Bio-Research Laboratories LTD, 1985a). Another developmental inhalation study in rats exposed to tripropylene glycol monomethyl ether aerosol from GD 6-15 reported a NOAEC of 1 mg/L-day (129 ppm), which is above tripropylene glycol monomethyl ether's theoretical air saturation vapor concentration of 7.88 ppm (Bio-Research Laboratories LTD, 1985b). Two studies where rats were exposed from GD 6-15 and rabbits were exposed from GD 7-19 to dipropylene glycol methyl ether

vapor both reported NOAECs of 0.45 mg/L (53 ppm), which is also above dipropylene glycol methyl ether's theoretical air saturation vapor concentration of 26 ppm (Reported to the ECHA database, 1990a, b). These results provide sufficient information to indicate low concern for developmental toxicity from vapor exposures based on no effects at air saturation and from aerosols by exceeding the low-concern benchmark of 0.5 mg/L for aerosol inhalation exposures.

6.1.5 Genotoxicity

EPA used experimental studies and read-across from analogs to assess tripropylene glycol-n-butyl ether's potential for gene mutations and chromosomal aberrations as potential indicators of genotoxic carcinogenicity.

One *in vitro* gene mutation study resulted in a negative finding with and without metabolic activation in *Salmonella typhimurium* exposed to tripropylene glycol-n-butyl ether (Reported to the ECHA database, 1989). Also, mice exposed to tripropylene glycol-n-butyl ether showed negative results in a micronuclei assay (Reported to the ECHA database, 1989).

EPA used read-across from analogs to assess genotoxicity through other mechanisms. Rat hepatocyte cells exposed to tripropylene glycol monomethyl ether did not elicit unscheduled DNA synthesis (Dow Chemical, 1982). Mice injected with dipropylene glycol monobutyl ether were negative for significant increases in the presence of micronuclei (OECD, 2003). Several studies on chromosomal aberrations in Chinese hamster ovary cells were available. Rat liver cells and Chinese hamster lung cells exposed to dipropylene glycol, methyl ether indicated negative results for chromosomal aberrations (Reported to the ECHA database, 2000b; Shell Chemical, 1983). Chinese hamster ovary cells exposed to dipropylene glycol monoethyl ether were also negative for chromosomal aberrations (Reported to the ECHA database, 1997). Chinese hamster ovary cells had mixed results for increases in chromosomal aberrations when exposed to dipropylene glycol monobutyl ether. One study reported negative results for inducing aberrations with and without activation (OECD, 2003). Two other studies reported dipropylene glycol monobutyl ether as positive for inducing chromosomal aberrations with and without activation; however, these results were observed at cytotoxic concentrations (OECD, 2003). Weighing the negative results in several cell lines with the positive results occurring only at cytotoxic concentrations, EPA interprets these results to provide sufficient information to indicate DPMA has low concern for inducing genotoxicity.

6.1.6 Carcinogenicity

Experimental data determined to be of adequate quality[31] on tripropylene glycol n-butyl ether or closely-related analogs were not reasonably available for the assessment of carcinogenicity potential. EPA used widely accepted new approach methodologies (NAMs), such as publicly available quantitative structure activity relationship (QSAR) models and structural alerts (SA) to assess the carcinogenic potential for tripropylene glycol n-butyl ether. Structural alerts represent molecular functional groups or substructures that are known to be linked to the carcinogenic activity of chemicals. The most common structural alerts are those for electrophiles (either direct acting or

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

following activation). Modulating factors that will impact the carcinogenic potential of a given electrophile will include its relative hardness or softness, its molecular flexibility or rigidity, and the balance between its reactivity and stability.[32]

For this chemical, there is an absence of the types of reactive structural features that are present in genotoxic carcinogens. Tripropylene glycol n-butyl ether is not an electrophile. ISS profiler, a QSAR model,[33] did not identify any alerts for the parent structure but did identify an aldehyde metabolite alert for a metabolite. However, this aldehyde is expected to be transient and further metabolized (see Figure 10 in the Metabolic Pathway Trees Supplemental Document[34]). Tripropylene glycol-n-butyl ether will undergo biotransformation through multiple other detoxification pathways, and subsequentially be excreted, making this alert of low concern (see Figure 10 in Metabolic Pathway Trees Supplemental Document). The Virtual models for property Evaluation of chemicals within a Global Architecture (VEGA) models'[35] results indicate tripropylene glycol n-butyl ether has low potential to be carcinogenic or mutagenic with moderate reliability.

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

6.1.7 Neurotoxicity

No guideline neurotoxicity studies on tripropylene glycol n-butyl ether or closely-related analogs were available to assess the potential for tripropylene glycol n-butyl ether to cause neurotoxicity. However, EPA assessed the potential for neurotoxicity using relevant endpoints measured in repeated dose studies and accepted NAMs, such as ToxCast.[36]

A repeated dose oral gavage study of dipropylene glycol monoethyl ether in rats reported minimal effects on the neurological endpoints that were evaluated (i.e., brain, sciatic nerve and spinal cord histopathology, field and motor activity measurements and a battery of neurobehavioral functions that were not described). Decreased hindlimb grip strength (magnitude of effect not reported) was observed in female rats at 1,000 mg/kg-day of dipropylene glycol monoethyl ether in a 90-day oral gavage study. Hindlimb grip strength was not affected by treatment in males from this study and no effects were noted in males or females during a 2-week recovery period. Dipropylene glycol monoethyl ether did not produce histopathological lesions in the brain, spinal cord and sciatic nerves or affect field or motor activity measurements (Reported to the ECHA database, 2000a).

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

[33] Carcinogenicity alerts by ISS 2.4 profiler as encoded in the QSAR Toolbox 4.3 qsartoolbox.org

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

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

[36] https://comptox.epa.gov/dashboard Chemical specific assay list can be found at https://comptox.epa.gov/dashboard/dsstoxdb/results?search=88917-22-0

A 13-week inhalation study of dipropylene glycol methyl ether in rats and rabbits did not report histopathological effects in the brain, peripheral nerve, or spinal cord in rats and rabbits at a concentration of 1.212 mg/L-day (Landry and Yano, 1984).

ToxCast results for tripropylene glycol n-butyl ether included 8 *in vitro* high throughout biochemical- and cell-based assays related to neurological functions.[37] Bioactivity was not induced in any assay by tripropylene glycol n-butyl ether.

Tripropylene glycol n-butyl ether's low-concern findings for other human health hazard endpoints, including acute, reproductive and developmental toxicity, and predictions by ToxCast, provide sufficient information to indicate low concern for neurotoxicity.

6.1.8 Skin Sensitization

Experimental data determined to be of adequate quality[38] on tripropylene glycol n-butyl ether or closely related analogs were not reasonably available for the assessment of skin sensitization potential. EPA used widely accepted NAMs which did not identify any structural alerts for protein binding potential of tripropylene glycol n-butyl ether in regard to skin sensitization, using the QSAR Toolbox, Version 4.2 models for protein binding potency h-CLAT; protein binding alerts for skin sensitization according to GHS; protein binding alerts for skin sensitization by OASIS; protein binding by OASIS; and protein binding by OECD. These results provide sufficient information to indicate low concern for skin sensitization.

6.1.9 Respiratory Sensitization

Experimental data determined to be of adequate quality[39] on tripropylene glycol n-butyl ether or closely related analogs were not reasonably available for the assessment of respiratory sensitization potential. To model respiratory sensitization for tripropylene glycol n-butyl ether, EPA used NAMs, such as the QSAR Toolbox, version 4.2 models[40] 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 tripropylene glycol n-butyl ether. The weight of scientific evidence provides sufficient information to indicate low concern for respiratory sensitization.

[37] Identified by supplemental information in 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

[38] The literature search and review process to determine studies of adequate quality for inclusion in the screening review is further discussed in the document "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.

[39] 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.

[40] 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

6.1.10 Immunotoxicity

EPA reviewed the literature for immunotoxicity endpoints such as lymphoid organ weight, histopathology, and immune function. 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. Changes to lymphoid tissue, such as the spleen or thymus, with accompanying histological changes or changes in hematological parameters can indicate potential for immunological toxicity. For tripropylene glycol n-butyl ether and the closely-related analogs, the included oral, inhalation, and dermal repeated dose studies did not report changes in these immunological parameters.

Some immunological effects were reported in the middle and high dose groups in a 13-week study of rats dermally exposed to the analog, dipropylene glycol monobutyl ether (OECD, 2003). For the study, the NOAEL was 91 mg/kg-day and LOAEL was 273 mg/kg-day based on increased neutrophil counts. Although effects were observed at doses close to the low-concern benchmark of 200 mg/kg-day, EPA does not consider hematological changes without accompanying organ and histopathological changes as adverse and does not classify these effects as an immunotoxicity outcome.

Based on the weight of the scientific evidence, these results provide sufficient information to indicate low concern for immunotoxicity from tripropylene glycol n-butyl ether.

6.1.11 Skin Irritation

EPA assessed dermal irritation effects using experimental data in rabbits. One study demonstrated tripropylene glycol n-butyl ether induced slight erythema in all three animals tested and edema in one of three animals, but these effects were reversible by day 7. Tripropylene glycol n-butyl ether was considered to be moderately irritating (Reported to the ECHA database, 1987b). Another study reported tripropylene glycol n-butyl ether slight erythema in three of three animals, but the result was fully reversible in 8 days (Reported to the ECHA database, 2001a). Due to the low severity and reversibility, these results indicate tripropylene glycol n-butyl ether is of moderate concern for skin irritation. The weight of the scientific evidence for these results is discussed in Section 8.1.

6.1.12 Eye Irritation

To assess potential for eye irritation, EPA used the results of two studies in rabbits. Rabbits exposed to tripropylene glycol n-butyl ether displayed slight eye irritation at 24 hours in the form of iris irritation, conjunctivae, and chemosis, but the effects were fully reversible by 14 days (Reported to the ECHA database, 1988d). Another study was negative for inducing eye irritation (Reported to the ECHA database, 2001c). Given the mixed results, these studies indicate tripropylene glycol n-butyl ether is of moderate concern for eye irritation. The weight of the scientific evidence for these results is discussed in Section 8.1.

6.1.13 Hazards to Potentially Exposed or Susceptible Subpopulations

The above information supports a low human health hazard finding for tripropylene glycol n-butyl ether 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 tripropylene glycol n-butyl ether.

6.2 Environmental Hazard

To review environmental hazard endpoints without adequate quality[28] 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 tripropylene glycol n-butyl ether based on available acute toxicity experimental data and estimated chronic toxicity values using the Ecological Structure Active (ECOSAR) Predictive Model.[41] Appendix B contains a summary of the reasonably available environmental hazard data.

6.2.1 Acute Aquatic Toxicity

EPA assessed environmental hazard from acute exposures to tripropylene glycol n-butyl ether using experimental data. Aquatic vertebrates exposed to tripropylene glycol n-butyl ether resulted in an LC_{50} of 564 mg/L (Reported to the ECHA database, 1988f, 1987a). Invertebrates exposed to tripropylene glycol n-butyl ether resulted in an EC_{50} greater than 100 mg/L (Reported to the ECHA database, 2002b, 1988e). Algae exposed to tripropylene glycol n-butyl ether resulted in EC_{50}s of 351 mg/L for cell volume and 265 mg/L for cell count (Reported to the ECHA database, 2009).These results 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 were estimated using ECOSAR. Chronic toxicity is predicted to occur at 72 mg/L for aquatic vertebrates, 35 mg/L for invertebrates, and 56 mg/L for algae. These predicted chronic toxicity values provide sufficient information to indicate that tripropylene glycol n-butyl ether 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

EPA assessed the environmental persistence for tripropylene glycol n-butyl ether using available experimental data on both ready biodegradation and inherent biodegradation.

Tripropylene glycol n-butyl ether passed two OECD 301-series ready tests and was considered readily biodegradable, meeting the 10-day window in the OECD 301F test (Dow Chemical, 1998; Reported to the ECHA database, 1998a), but did not meet the 10-day window in the OECD 301A test (Reported to the ECHA database, 2002a). An inherent biodegradability test OECD 302B (Reported to the ECHA database, 1993) provides additional evidence that tripropylene glycol n-butyl ether is inherently and ultimately biodegradable. Furthermore, the microbial inhibition tests indicate that this substance is non-toxic to microbial populations found in sewage treatment plants (Reported to the ECHA database, 2001d).

Anaerobic biodegradation data were not available for tripropylene glycol n-butyl ether; however, an anaerobic study was available in a closely related analog. In an OECD 311 equivalent test, the analog

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

dipropylene glycol methyl ether degraded 10% by gas volume after 81 days under anaerobic conditions in municipal digester sludge (Reported to the ECHA database, 1998b). The method used in the OECD 311 Guideline study and in BIOWIN modeling predictions is based on the ISO 11734 anaerobic test[42], a test used to describe methanogenic anaerobic biodegradation. Methanogenic anaerobic biodegradation is only one of several known anaerobic biodegradation pathways in anoxic environments. Other pathways include manganese and iron reduction, sulfate-reducing microorganisms, and halorespiring bacteria (Ghattas et al. 2017)[43]. For tripropylene glycol n-butyl ether, the chemical substance contains degradable functional groups such as primary alcohols and propylene glycols. Primary alcohols can be converted to carboxylic acid under methanogenic conditions (Ghattas et al., 2017)[43]. Small propylene glycols may also undergo methanogenic fermentation following a disproportionation reaction and these fermentation products can then degrade via anaerobic oxidation reactions (Veltman et al. 1998)[44]. While EPA cannot be certain of the rates at which these anerobic pathways may occur, tripropylene glycol n-butyl ether's structure contains functional groups that have been documented in the literature as having potential to undergo anaerobic biodegradation.

Based on the available information, the experimental data indicate that tripropylene glycol n-butyl ether is readily biodegradable under aerobic conditions, and complete mineralization of this chemical has been reported using both standard and non-standard test methods. No degradation products of concern were identified for this chemical substance. Applying expert scientific judgement based on the reasonably available information and weight of scientific evidence, EPA has sufficient information that this chemical will have low persistence.

6.3.2 Bioaccumulation Potential

Based on the estimated bioaccumulation factor (BAF) value of 6.22 using the Estimation Programs Interface (EPI) Suite models,[45] EPA has sufficient information that tripropylene glycol n-butyl ether has low potential for bioaccumulation in the environment based on the low-concern benchmark of less than 1000.

[42] ISO 11734 is a screening method for the evaluation of potential anerobic biodegradability of organic chemicals under a specific condition (i.e. in an anaerobic digester at a given time and range of concentration[s] of micro-organisms. The Guideline notes, "because a diluted sludge is used with a relatively high concentration of a test substance and the duration of the test typically is longer than the retention time in anaerobic digesters, the conditions of the test do not necessarily correspond to the conditions in anaerobic digesters, nor is it applicable for the assessment of anaerobic biodegradability of organic chemicals under different environmental conditions" and that "substances which fail to be converted to gas in the test may not necessarily persist at more environmentally realistic substance-to-biomass ratios." (https://www.oecd-ilibrary.org/docserver/9789264016842-en.pdf?expires=1577971707&id=id&accname=guest&checksum=BFC045C3905F4F985EB5BC3C0934B655)

[43] 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

[44] 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

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

7. Exposure Characterization

EPA considered reasonably available information on exposure for tripropylene glycol n-butyl ether. In general, there is limited information on exposure for low hazard chemicals. EPA consulted sources of use information that include CDR and other databases and public sources. EPA used these sources (described in Table A.2) to inform the Agency's understanding of intended, known, or reasonably foreseen uses (Section 5).

As shown in Tables 3 and A.3, tripropylene glycol n-butyl ether is a solvent used in processing (incorporation into an article and into a formulation, mixture, or product), as a plasticizer, and in cleaning products, as well as in ink, toner, and colorant products (among others) for consumer and commercial use. It is used in a variety of industrial, consumer, and commercial uses. Non-TSCA uses, including those excluded under TSCA section 3(2), are beyond the scope of this assessment (See Table A.3).

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

7.1 Production Volume Information

Production volume information for tripropylene glycol n-butyl ether is based on an analysis of the CDR from 1986 to 2015.[46] From 1986 to 1994 reporting years, no data was reported for the aggregate production volume of tripropylene glycol n-butyl ether. This does not mean it was not being produced or imported, but more likely that no single entity site was producing above the reporting threshold of generally 25,000 lbs. For the 1998 reporting year, the aggregate production volume of tripropylene glycol n-butyl ether was between 500,000 and 1,000,000 lbs. From 2002 to 2015 reporting years, the aggregate production volume of tripropylene glycol n-butyl ether was between 1,000,000 and 10,000,000 lbs. For the 2011 reporting, aggregate production volume information was withheld. In general, since 2012, production volume has remained relatively stable without significant increases or decreases.

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 tripropylene glycol n-butyl ether. Exposure is also reasonably foreseen from other uses, such as distribution and disposal. These activities could result in releases of tripropylene glycol n-butyl ether to media including surface water, landfills, and air.

EPA expects high levels of removal of tripropylene glycol n-butyl ether 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, tripropylene glycol n-butyl ether 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

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

this chemical to surface water 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} (Section 3), tripropylene glycol n-butyl ether is expected to have negligible adsorption to sediment, reducing the potential toxicity to benthic organisms. Tripropylene glycol n-butyl ether'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 and anaerobic conditions (aerobic and anaerobic biodegradation are discussed in Section 6.3.1).

If incineration releases during manufacturing and processing occur, EPA expects significant degradation of tripropylene glycol n-butyl ether to the point that it will not be present in air.

7.3 Exposures to the General Population

EPA expects the general population could be exposed to tripropylene glycol n-butyl ether from the potential environmental releases described above. Air exposure is unlikely from incineration. If tripropylene glycol n-butyl ether is present in the air from volatilization, it is expected to be reduced because of its short atmospheric half-life of less than 2 hours (Table 2). With the exception of time immediately following a release, tripropylene glycol n-butyl ether 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. Given the low bioaccumulation or bioconcentration potential of tripropylene glycol n-butyl ether, oral exposure to tripropylene glycol n-butyl ether via fish ingestion is unlikely.

7.4 Exposures to Potentially Exposed or Susceptible Subpopulations

EPA identified workers as potentially exposed or susceptible subpopulations based on greater exposure to tripropylene glycol n-butyl ether than the general population during manufacturing, processing, distribution, use, and disposal. EPA identified consumers as a population that may experience greater exposure to tripropylene glycol n-butyl ether than the general population through use of ink, toner, and colorant products; anti-freeze and de-icing products; and cleaning and furnishing care products, for example.

7.4.1 Exposures to Workers

Based on its reported physical form and measured melting point (Table 2), tripropylene glycol n-butyl ether is a liquid under ambient conditions. Based on tripropylene glycol n-butyl ether's conditions of use (Table 3), workers may be exposed to liquids through direct dermal contact with the substance and inhalation of aerosols if they are generated. Based on its measured vapor pressure, tripropylene glycol n-butyl ether is expected to be volatile at ambient temperatures, and therefore workers may be exposed through inhalation of vapors. However, if tripropylene glycol n-butyl ether is in a dilute form, the estimated Henry's Law constant for tripropylene glycol n-butyl ether suggests volatilization from water and aqueous solutions is expected to be minimal. Workers may be exposed to tripropylene glycol n-butyl ether in manufacturing, processing, distribution, industrial use, and disposal.

7.4.2 Exposures to Consumers

Consumers could be exposed to tripropylene glycol n-butyl ether through the use of ink, toner, and colorant products, cleaning and furnishing care products; and anti-freeze and de-icing products, among others (Table 3). For all these uses, if dermal contact does occur, tripropylene glycol n-butyl ether is expected to have poor to moderate absorption through the skin based on its molecular weight, water solubility and partitioning coefficients (Section 3). If the chemical is in an aerosol product and inhalation exposure occurs, tripropylene glycol n-butyl ether'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 likely conditions of use that could lead to an exposure (82 FR 33726). Thus, oral exposures will be incidental (meaning inadvertent and low in volume). Tripropylene glycol n-butyl ether is expected to be metabolized and excreted, further reducing the duration of exposure.

8. Summary of Findings

EPA has used reasonably available information on the following statutory and regulatory criteria and considerations to screen tripropylene glycol n-butyl ether 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 tripropylene glycol n-butyl ether. EPA used this information to inform its determination of whether tripropylene glycol n-butyl ether meets the statutory criteria and considerations for final designation as a low-priority substance.

- **Hazard potential:**

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

- **Exposure potential:**

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

children, and consumers (discussed in Sections 3 and 7). EPA also gathered information on environmental releases. EPA identified workers, the general population, consumers, and the environment as most likely to experience exposures. EPA determined that while the general population, workers and consumers may be exposed to tripropylene glycol n-butyl ether, exposure by the dermal pathway is limited by tripropylene glycol n-butyl ether's physical-chemical properties. If ingestion occurs, tripropylene glycol n-butyl ether is expected to be metabolized and excreted, reducing the duration of exposure. Inhalation of tripropylene glycol n-butyl ether in dilute products is expected to be minimal; however, workers may be exposed to vapors of this chemical in neat form. If tripropylene glycol n-butyl ether is released into the environment, its exposure potential will be reduced through biodegradation.

Rationale: Although tripropylene glycol n-butyl ether may cause moderate eye and skin irritation, the effects are expected to be relatively low-impact [minimal to moderate] and reversible, thereby reducing concern for longer-term effects. TSCA conditions of use would be unlikely to result in frequent eye exposure because use patterns do not involve intentional eye or skin exposure for occupational scenarios. Workers could be exposed during processing, manufacturing, distribution, use, and disposal through splashing or hand-to-face and eye contact. Other uses covered under TSCA, such as consumer uses in cleaning and furnishing care products, would be unlikely to result in more than incidental skin and eye exposure. Eye and skin irritation resulting from exposure in an occupational and consumer setting is mitigated by the reversible nature of the effects and furthermore by the strong likelihood that any exposures would be self-limiting, especially by those who experience irritation from exposure.

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 tripropylene glycol n-butyl ether 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 tripropylene glycol n-butyl ether based on a set of EPA and internationally accepted measurement tools and benchmarks that are indicators of persistence and bioaccumulation potential (described in Section 6). These endpoints are key components in evaluating a chemical's persistence and bioaccumulation potential.

Rationale: EPA review of experimental data indicates tripropylene glycol n-butyl ether is readily biodegradable under aerobic conditions, with greater than 60 percent biodegradation expected within 28 days. EPA's EPI Suite models indicate a low potential for bioaccumulation and bioconcentration.

Conclusion: Based on an initial screen of reasonably available information on persistence and bioaccumulation, EPA concludes that the screening-level review under 40 CFR 702.9(a)(2) does not support a finding that tripropylene glycol n-butyl ether 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, use, and disposal of tripropylene glycol n-butyl ether as a potentially exposed or susceptible subpopulation (described in more detail in Section 7). EPA also identified consumers as a potentially exposed subpopulation because of their use of ink, toner, and colorant products, cleaning and furnishing care products, and other types of products.

Rationale: EPA did not identify hazard effects for this chemical that would make any population susceptible. EPA expects workers and consumers to have a higher exposure to tripropylene glycol n-butyl ether than the general population. Because of the chemical's low-concern hazard properties and reversibility of the effects, this exposure does not pose a significant increase in risk for workers or consumers.

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 tripropylene glycol n-butyl ether 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 tripropylene glycol n-butyl ether 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 tripropylene glycol n-butyl ether 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, tripropylene glycol n-butyl ether 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, tripropylene glycol n-butyl ether 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 tripropylene glycol n-butyl ether 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.

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, tripropylene glycol n-butyl ether 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 tripropylene glycol n-butyl ether 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 tripropylene glycol n-butyl ether under 40 CFR 702.9(a)(4) does not support a finding that tripropylene glycol n-butyl ether 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 tripropylene glycol n-butyl ether and related potential exposures and hazards.

Rationale: EPA evaluated the conditions of use of tripropylene glycol n-butyl ether (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-level review would likely not change and would not alter the Agency's conclusion of low concern. EPA bases this expectation on tripropylene glycol n-butyl ether'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 tripropylene glycol n-butyl ether 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 tripropylene glycol n-butyl ether 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 tripropylene glycol n-butyl ether (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 tripropylene glycol n-butyl ether as a low-priority substance could result in increased use and higher production volumes. EPA expects, however, that any changes in tripropylene glycol n-butyl ether'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 tripropylene glycol n-butyl ether'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, tripropylene glycol n-butyl ether 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-level review to support the final designation of tripropylene glycol n-butyl ether 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 tripropylene glycol n-butyl ether 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 tripropylene glycol n-butyl ether as a low-priority substance.

Appendix A: Conditions of Use Characterization

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

A.1 CDR Manufacturers and Production Volume

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

Table A.1 presents the historic production volume of tripropylene glycol n-butyl ether from the CDR (previously known as the Inventory Update Rule, or IUR) from 1986-2015. From 1986 to 1994 reporting years, no data was reported for the aggregate production volume of tripropylene glycol n-butyl ether. This does not mean it was not being produced or imported, but more likely that no single entity site was producing above the reporting threshold. For the 1998 reporting year, the aggregate production volume of tripropylene glycol n-butyl ether was between 500,000 and 1,000,000 lbs. From 2002 to 2015 reporting years, the aggregate production volume of tripropylene glycol n-butyl ether was between 1,000,000 and 10,000,000 lbs. For the 2011 reporting, aggregate production volume information was withheld. In general, since 2012, production volume has remained relatively stable without significant increases or decreases.

Table A.1: 1986-2015 National Production Volume Data for Tripropylene Glycol n-Butyl Ether (Non-Confidential Production Volume in Pounds)

1986	1990	1994	1998	2002	2006	2011	2012	2013	2014	2015
NDR	NDR	NDR	500 K – 1M	1 M – 10 M	1 M – 10 M	Withheld	1 M – 10 M	1 M – 10 M	1 M – 10 M	1 M – 10 M

Source(s):
EPA (2002; 2006; 2017b; 2018a)
Note(s):
K = Thousand; M = Million; NDR = No data reported

A.2 Uses

A.2.1 Methods for Uses Table

Section A.1 provides a list of known uses of tripropylene glycol n-butyl ether, 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 Tripropylene Glycol n Butyl Ether

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)	55934-93-5	No
Canada Chemicals Management Plan information sheets	Government of Canada (2018)	Tripropylene glycol n-butyl ether	No
Chemical and Product Categories (CPCat)	CPCat (2019)	55934-93-5	Yes
ChemView [2]	EPA (2018a)	55934-93-5	Yes
Children's Safe Product Act Reported Data	Washington State Dept. of Ecology (2018)	55934-93-5	No
Consumer Product Information Database (CPID)	DeLima Associates (2018a)	55934-93-5	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)	Tripropylene glycol n-butyl ether	No
DrugBank	DrugBank (2018)	55934-93-5	No
European Chemicals Agency (ECHA) Registration Dossier	ECHA (2018)	55934-93-5	Yes
eChemPortal [2]	OECD (2018)	55934-93-5	No
Envirofacts [2]	EPA (2018b)	55934-93-5	No
Functional Use Database (FUse)	EPA (2017a)	55934-93-5	Yes
Kirk-Othmer Encyclopedia of Chemical Technology	Kirk-Othmer (2006)	Tripropylene glycol n-butyl ether; Tripropylene glycol monobutyl ether	No
Non-Confidential 2016 Chemical Data Reporting (CDR)	EPA (2017b)	55934-93-5	Yes
PubChem Compound	Kim et al. (2016)	55934-93-5	Yes

Table A.2: Sources Searched for Uses of Tripropylene Glycol n Butyl Ether			
Title	**Author and Year**	**Search Term(s)**	**Found Use Information? [1]**
Safer Chemical Ingredients List (SCIL)	EPA (2018d)	55934-93-5	Yes
Synapse Information Resources [2]	Synapse Information Resources (2009)	Tripropylene glycol n-butyl ether	Yes
Resource Conservation and Recovery Act	EPA (2018c)	Tripropylene glycol n-butyl ether; Tripropylene glycol butyl ether;	No
Scorecard: The Pollution Information Site	GoodGuide (2011)	55934-93-5	No
Skin Deep Cosmetics Database	EWG (2018)	55934-93-5	No
Toxics Release Inventory (TRI)	EPA (2018e)	55934-93-5	No
TOXNET [2]	NLM (2018a)	55934-93-5	Yes
Ullmann's Encyclopedia of Industrial Chemistry	Ullmann's (2000)	Tripropylene glycol n-butyl ether; Tripropylene glycol monobutyl ether	No
Additional sources identified from reasonably available information			
CLR Brands	CLR Brands (2018a)	Incidentally identified while researching details of this chemical's uses and products.	Yes
Note(s): 1. If use information was found in the resource, it will appear in Table unless otherwise noted. 2. This source is a group of databases; thus the exact resource(s) it led to will be cited instead of the database as whole.			

The U.S. Patent and Trademark Office has an online database that shows 526 patents referencing "tripropylene glycol n-butyl ether" (USPTO 2018). Although patents could be useful in determining reasonably foreseen uses, it is difficult to confirm whether any of the patented technologies are currently in use. Uses inferred from patents containing tripropylene glycol n-butyl ether 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 Tripropylene Glycol n-butyl Ether

Table A.3: Uses of Tripropylene Glycol n-Butyl Ether		
Use	**Expected Users**	**Description of Use and References**
TSCA Conditions of Use: Cleaning and Furnishing Care Products CDR reports use of tripropylene glycol n-butyl ether in consumer cleaning and furnishing care products at concentrations of at least 1 percent but less than 30 percent by weight (EPA 2017b).		
Air care products	Consumer	Reported to the ECHA database (2018) The ECHA registration dossiers lists the use tripropylene glycol n-butyl ether in air care products. ECHA does not expand on this use, however this category generally includes products such as air fresheners, candles, and scented gels. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are consumer based on inclusion in ECHA's consumer uses.
Bath cleaner	Consumer, commercial	CLR Brands (2018a) Tripropylene glycol n-butyl ether is listed as an ingredient in consumer and commercial bathroom cleaner products, for grout and tile, sinks and toilets. Expected users are consumer and commercial, as the product is available for consumer and commercial use.
Descalers	Consumer, commercial	CLR Brands (2018f); CLR Brands (2018b) Tripropylene glycol n-butyl ether is listed as an ingredient in a descalers such as kitchen, lime and rust remover products. Expected users are consumer and commercial, as the products is available for use in both consumer and commercial settings.

Table A.3: Uses of Tripropylene Glycol n-Butyl Ether		
Use	**Expected Users**	**Description of Use and References**
Cleaning/ washing agent	Consumer, commercial, industrial	CPCat (2019); Reported to the ECHA database (2018) CPCat lists the use of tripropylene glycol n-butyl ether in cleaning and washing agents. The ECHA registration dossier indicates the use of tripropylene glycol n-butyl ether in washing and cleaning products/ agents. Expected users are consumer, commercial, and industrial based on inclusion in ECHA's consumer uses, uses by professional workers, and uses at industrial sites.
Degreaser	Consumer, commercial	CPCat (2019) CPCat lists the use of tripropylene glycol n-butyl ether in "degreasers (cold degreasing, de-waxing, de-polishing)."
Hardwood floor finish	Consumer	DeLima Associates (2018b) CPID generally includes products for consumer use; therefore the expected user is a consumer.
Kitchen cleaner	Consumer, commercial	CLR Brands (2018c) Tripropylene glycol n-butyl ether is listed as an ingredient in consumer and commercial kitchen cleaner products Expected users are consumer and commercial, as the product is available for consumer and commercial use.
Metal cleaner/ polish	Commercial	CLR Brands (2018d) Tripropylene glycol n-butyl ether is listed as an ingredient in a commercial metal cleaning product. Expected users are commercial, as the product is available for commercial use.

Table A.3: Uses of Tripropylene Glycol n-Butyl Ether		
Use	**Expected Users**	**Description of Use and References**
Mold and mildew stain remover	Consumer, commercial	CLR Brands (2018g) Tripropylene glycol n-butyl ether is listed as an ingredient in mold and mildew stain remover products. Expected users are consumer and commercial, as the products is available for use in both consumer and commercial settings.
Multi-surface cleaner	Consumer	CLR Brands (2018e) Tripropylene glycol n-butyl ether is listed as an ingredient in a kitchen and multi-surface cleaner currently available for use. Expected users are consumer, as the product is available for consumer use.
TSCA Conditions of Use: Industrial Uses		
Coatings	Industrial	Reported to the ECHA database (2018) The ECHA registration dossier lists the use tripropylene glycol n-butyl ether in coatings used for various industrial processes and products including chemical and in industrial spraying. Expected users are industrial based on inclusion in ECHA's uses at industrial sites.
Construction	Industrial	CPCat (2019) CPCat lists the use of tripropylene glycol n-butyl ether in construction materials and in the construction of buildings. Expected users are industrial based on CDR's Industrial Processing and Use report.

Table A.3: Uses of Tripropylene Glycol n-Butyl Ether		
Use	**Expected Users**	**Description of Use and References**
Metal working fluids	Commercial, industrial	Reported to the ECHA database (2018) The ECHA registration dossiers lists the use tripropylene glycol n-butyl ether in "metal working fluids/ rolling oils." It is unknown if use is ongoing in the United States. Expected users are commercial and industrial based on inclusion in ECHA's uses by professional workers and uses at industrial sites.
Mining chemicals	Industrial	Reported to the ECHA database (2018) The ECHA registration dossier lists the use of tripropylene glycol n-butyl ether in mining chemicals. No further information could be found on this use in the United States. Expected users are industrial based on inclusion in ECHA's uses at industrial sites.
Oil and gas drilling	Industrial	Reported to the ECHA database (2018) The ECHA registration dossier lists the use of tripropylene glycol n-butyl ether in oil and gas field drilling and production operations. No further information could be found on this use in the United States. Expected users are industrial based on inclusion in ECHA's uses at industrial sites.
Wholesale and retail trade	Industrial	EPA (2017b) CDR reports use of tripropylene glycol n-butyl ether as a plasticizer in wholesale and retail trade. No further information could be found on this specific use. Expected users are industrial based on CDR's Industrial Processing and Use report.

Table A.3: Uses of Tripropylene Glycol n-Butyl Ether		
Use	**Expected Users**	**Description of Use and References**
TSCA Conditions of Use: Manufacturing		
Chemical manufacturing	Industrial	EPA (2017b); CPCat (2019); Reported to the ECHA database (2018) CDR reports use of tripropylene glycol n-butyl ether as a solvent and processing aid in "chemical product and preparation manufacturing" and in "other basic organic chemical manufacturing" at concentrations of at least percent by weight. CPCat lists the use of tripropylene glycol n-butyl ether in chemical, chemical products, and basic organic chemical manufacturing. The ECHA registration dossier lists the use of tripropylene glycol n-butyl ether as an intermediate in the manufacture of "bulk, large scale chemical (including petroleum products)" and fine chemicals. Expected users are industrial based on CDR's Industrial Processing and Use report.
Communication equipment manufacturing	Industrial	CPCat (2019) CPCat lists the use of tripropylene glycol n-butyl ether in the manufacture of "radio, television and communication equipment." Expected users are industrial based on CPCat's user classification.
Electrical manufacturing	Industrial	CPCat (2019) CPCat lists the use of tripropylene glycol n-butyl ether in the manufacture of electrical machinery, apparatus and optical equipment. Expected users are industrial based on CPCat's user classification.
Fabricated metal product manufacturing	Industrial	CPCat (2019) CPCat lists the use of tripropylene glycol n-butyl ether in the manufacture of "fabricated metal products, except machinery." Expected users are industrial based on CPCat's user classification.

Table A.3: Uses of Tripropylene Glycol n-Butyl Ether		
Use	**Expected Users**	**Description of Use and References**
Furniture manufacturing	Industrial	CPCat (2019) CPCat lists the use of tripropylene glycol n-butyl ether in the manufacture of furniture, and in industrial varnishing and acid washing of furniture. Expected users are industrial based on CPCat's user classification.
Paint manufacturing	Industrial	CPCat (2019) CPCat lists the use of tripropylene glycol n-butyl ether in the manufacture of "paints, varnishes, and similar coatings, print." Expected users are industrial based on CPCat's user classification.
Wood manufacturing	Industrial	CPCat (2019) CPCat lists the use of tripropylene glycol n-butyl ether in the manufacture of "wood and products of wood and cork." Expected users are industrial based on CPCat's user classification.
TSCA Conditions of Use: Pesticides and Agriculture		
Agrochemicals	Commercial	Reported to the ECHA database (2018) The ECHA registration dossiers lists the use tripropylene glycol n-butyl ether in agrochemicals. It is unknown if use is ongoing in the United States. Expected users are commercial based on inclusion in ECHA's uses by professional workers.
Inert ingredient	Unknown	CPCat (2019) CPCat lists the use of tripropylene glycol n-butyl ether as an inert ingredient in pesticides. Expected users are unknown, due to the limited availability of information.

Table A.3: Uses of Tripropylene Glycol n-Butyl Ether		
Use	**Expected Users**	**Description of Use and References**
TSCA Conditions of Use: Miscellaneous		
Adhesives and sealants	Consumer	Reported to the ECHA database (2018) The ECHA registration dossiers lists the use tripropylene glycol n-butyl ether in adhesives and sealants. It is unknown if use is ongoing in the United States. Expected users are consumer based on inclusion in ECHA's consumer uses.
Anti-freeze and deicing products	Consumer	Reported to the ECHA database (2018) The ECHA registration dossiers lists the use tripropylene glycol n-butyl ether in anti-freeze and de-icing products. It is unknown if use is ongoing in the United States. Expected users are consumer based on inclusion in ECHA's consumer uses.
Inks and toners	Consumer	Reported to the ECHA database (2018) The ECHA registration dossiers lists the use tripropylene glycol n-butyl ether in inks and toners. It is unknown if use is ongoing in the United States. Expected users are consumer based on inclusion in ECHA's consumer uses.
Leather treatment products	Consumer	Reported to the ECHA database (2018) The ECHA registration dossiers lists the use tripropylene glycol n-butyl ether in leather treatment products. It is unknown if use is ongoing in the United States. Expected users are consumer based on inclusion in ECHA's consumer uses.
Lubricants and greases	Consumer	Reported to the ECHA database (2018) The ECHA registration dossiers lists the use tripropylene glycol n-butyl ether in "lubricants, greases, release products." It is unknown if use is ongoing in the United States. Expected users are consumer based on inclusion in ECHA's consumer uses.

Table A.3: Uses of Tripropylene Glycol n-Butyl Ether		
Use	**Expected Users**	**Description of Use and References**
Non-metal surface treatment products	Consumer	Reported to the ECHA database (2018) The ECHA registration dossiers lists the use tripropylene glycol n-butyl ether in non-metal surface treatment products. It is unknown if use is ongoing in the United States. Expected users are consumer based on inclusion in ECHA's consumer uses.
Paint, lacquers, coatings, varnishes	Consumer, commercial	CPCat (2019); Reported to the ECHA database (2018) CPCat lists the use of tripropylene glycol n-butyl ether in paints, lacquers and varnishes, including water based, thinners, decorative, and protective exterior. The ECHA dossier lists the use of tripropylene glycol n-butyl ether in coatings and paints, thinner and painter removes. Expected users are consumer and commercial based on inclusion in ECHA's consumer uses and uses by professional workers.
Perfumes and fragrances	Consumer	Reported to the ECHA database (2018) The ECHA registration dossiers lists the use tripropylene glycol n-butyl ether in perfumes and fragrances. It is unknown if use is ongoing in the United States. Expected users are consumer based on inclusion in ECHA's consumer uses.
Polishes and wax blends	Consumer	Reported to the ECHA database (2018) The ECHA registration dossiers lists the use tripropylene glycol n-butyl ether in polishes and wax blends. It is unknown if use is ongoing in the United States. Expected users are consumer based on inclusion in ECHA's consumer uses.

Table A.3: Uses of Tripropylene Glycol n-Butyl Ether		
Use		**Description of Use and References**
Textile dyes	Consumer	Reported to the ECHA database (2018) The ECHA registration dossiers lists the use tripropylene glycol n-butyl ether in "textile dyes, and impregnating products." It is unknown if use is ongoing in the United States. Expected users are consumer based on inclusion in ECHA' consumer uses.
Welding and soldering products	Consumer	Reported to the ECHA database (2018) The ECHA registration dossiers lists the use tripropylene glycol n-butyl ether in "welding and soldering products, flux products." It is unknown if use is ongoing in the United States. Expected users are consumer based on inclusion in ECHA's consumer uses.
Non-TSCA Uses		
Biocides	Consumer	Reported to the ECHA database (2018) The ECHA registration dossiers lists the use tripropylene glycol n-butyl ether in biocidal products such disinfectants and for pest control. It is unknown if use is ongoing in the United States. Expected users are consumer based on inclusion in ECHA"s consumer uses.
Cosmetics, personal care products	Consumer	Reported to the ECHA database (2018) The ECHA registration dossiers lists the use tripropylene glycol n-butyl ether in cosmetics, personal care products. More specific uses within this use category were not listed, therefore it is unknown if this is an ongoing use in the Unity States. Expected users are consumer based on inclusion in ECHA's consumer uses.
Children's Products		
CDR reports did not include any uses in children's products.		
Recycling and Disposal		
In the 2016 CDR, three facilities reported that the chemical was not recycled, and one facility reported this information as CBI. (EPA 2017b)		

A.3 References

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Appendix B: Hazard Characterization

Table B.1: Human Health Hazard

Acute Mammalian Toxicity

Source	Exposure Route	Species & strain (if available)	Duration	Doses and replicate number	Effect	Study Details
5178571	Oral (gavage)	Wistar rats	Single exposure,14 day observation	**Doses:** 2400, 3200, and 4200 mg/kg **Replicates:** 5 per sex per dose	**LD_{50}:** 2800 mg/kg	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity: 99% • OECD Guideline 401 • GLP compliant **Mortality Results:** • 3/10 in 2400 mg/kg dose • 6/10 in 3200 mg/kg dose • 10/10 in 4200 mg/kg dose
5178572	Oral	Fisher 344 rats	Single exposure,14 day observation	**Dose:** 2000 mg/kg **Replicates:** 3 females	**LD_{50}** > 2000 mg/kg	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity: 85% • OECD Guideline 401 • GLP compliance not reported **Mortality Results:** • 1/3 animals
5178576	Oral (gavage)	Wistar rats	Single exposure	**Dose:** 2000 mg/kg **Replicates:** 6 per sex	**LD_{50}** > 2000 mg/kg	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity not reported • OECD Guideline 423 • GLP compliant **Mortality Results:** • 1/12 animals
5178577	Dermal	Wistar rats	25 hour exposure, 14 day observation	**Dose:** 2000 mg/kg **Replicates:** 5 per sex	**LD_{50}** > 2000 mg/kg	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity: 99% • OECD Guideline 402 • GLP compliant

Table B.1: Human Health Hazard						
						Mortality Results: • No mortalities
4956637, 5015984	Inhalation	Fischer 344 rats	4 hour exposure, 14 day observation	**Doses:** 0 and 5.7 mg/L **Replicates:** 6 males per group	**LC_{50}** > 5.7 mg/L	**Methods** • Test substance reported as CASRN 88917-22-0 • Purity not reported • Equivalent to OECD Guideline 403 • GLP compliant **Mortality Results:** • No mortalities
Repeated Dose Toxicity						
Source	**Exposure Route**	**Species & strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
5178575	Oral (gavage)	Fischer 344 rats	28 days	**Doses:** 0, 100, 350 and 1000 mg/kg-day **Replicates:** 5 per sex per dose	**NOAEL:** 100 mg/kg-day **LOAEL:** 350 mg/kg-day based on increased liver weight and enlarged hepatocyte	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity: 80.67% • OECD Guideline 407 • GLP compliant
5178581	Oral (drinking water)	Fischer 344 rats	13 weeks	**Doses:** 0, 100, 350 and 1000 mg/kg-day **Replicates (by dose):** • 0 mg/kg-day: 20 per sex • 100 mg/kg-day: 10 per sex • 350 mg/kg-day: 10 per sex • 1000 mg/kg-day: 20 per sex	**NOAEL:** 350 mg/kg-day **LOAEL:** 1000 mg/kg-day based on increased liver and kidney weights	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity: 97.7% • OECD Guideline 408 • GLP compliant • 10/20 animals in the 0 mg/kg-day and 1000 mg/kg-day groups were given a 4-week recovery period

Table B.1: Human Health Hazard						
3041622, 4944882	Dermal	Rabbits	90 days	**Doses:** 0, 950, 2850, 4750, and 9500 mg/kg-day **Replicates:** 5-7 males per group	**NOAEL:** 4750 mg/kg-day **LOAEL:** 9500 mg/kg-day based on increased mortality	**Methods:** • Test substance reported as CASRN 34590-94-8 • Purity not reported; test substance was presumably undiluted • Doses reported in mL/kg-day; converted to mg/kg-day based on a density of 0.95 g/mL • GLP compliance not reported
4146480	Dermal	Porton-Wistar rats	28 days	**Doses:** 0, 100, and 1000 mg/kg **Replicates:** 8 males per group	**NOAEL:**1000 mg/kg; equivalent to an adjusted daily dose of 714 mg/kg/day	**Methods:** • Test substance reported as CASRN 34590-94-8 • Purity not reported • GLP compliance not reported
5077871	Dermal	Rabbits	90 days	**Doses:** 0, 2850, and 4750 mg/kg-day **Replicates:** 5 males per group	**NOAEL:** 4750 mg/kg-day	**Methods:** • Test substance reported as CASRN 34590-94-8 • Purity not reported • GLP compliance not reported
4956637	Dermal	Wistar rats	13 weeks	**Doses:** 0, 91, 273, and 910 mg/kg-day **Replicates:** 10 per sex per group	**NOAEL:** 91 mg/kg-day **LOAEL:** 273 mg/kg-day based on decreased body weights in males and increased white blood cell counts in both sexes	**Methods:** • Test substance reported as CASRN 29911-28-2 • Purity > 95% • GLP compliant
4944882, 5077872, 4956637	Dermal	Rabbits	90 days	**Doses:** 0, 960, 2900, 4,800, and 9600 mg/kg-day **Replicates:** 5-8 males per group	**NOAEL:** 960 mg/kg-day **LOAEL**: 2900 mg/kg-day based on decreased body weight and increased kidney weight	**Methods:** • Test substance reported as CASRN 25498-49-1 • Purity not reported • GLP compliance not reported • Doses reported in mL/kg-day; converted to mg/kg-day based on a density of 0.96 g/mL
4946620	Inhalation	Fisher 344 rats	13 weeks	**Doses:** 0, 0.091, 0.393, and 1.212 mg/L-day **Replicates:** 10 per sex per group	**NOAEC:** 1.212 mg/L-day	**Methods:** • Test substance reported as CASRN 34590-94-8 • Purity: 99% • GLP compliance not reported

Table B.1: Human Health Hazard						
4946620	Inhalation	New Zealand White rabbits	13 weeks	**Doses:** 0, 0.091, 0.393, and 1.212 mg/L-day **Replicates:** 7 per sex per group	**NOAEC:** 1.212 mg/L-day	**Methods:** • Test substance reported as CASRN 34590-94-8 • Purity: 99% • GLP compliance not reported
Reproductive Toxicity						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
5077928	Oral (gavage)	Sprague-Dawley rats	1 generation	**Doses:** 0, 50, 225, and 1000 mg/kg-day **Replicates:** 32 per sex per dose	**NOAEL:** 1000 mg/kg-day	**Methods:** • Test substance reported as CASRN 30025-38-8 • Purity 90.15% • OECD Guideline 415 • GLP compliant **Results:** • No effects on fertility, gestation or parturition in P0. • No effects in offspring viability, and no physical or behavioral anomalies in pups.
Developmental Toxicity						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
4956637	Dermal	Wistar-derived SPF-bred albino rats	GD 6-15	**Doses:** 0, 273, and 910 mg/kg-day **Replicates:** 21-25 females per dose	**NOAEL:** 910 mg/kg-day	**Methods:** • Test substance reported as CASRN 29911-28-2 • Purity > 95% • OECD Guideline 414 • GLP compliant
5077931	Inhalation	New Zealand White rabbits	GD 7-19	**Doses:** 0.076, 0.23, and 0.45 mg/L for 6 hours per day **Replicates:** 16 females per dose	**NOAEC:** 0.45 mg/L-day	**Methods:** • Test substance reported as CASRN 34590-94-8 • Purity 100% • EPA OTS 798.4350 • GLP compliant

Table B.1: Human Health Hazard						
5077930	Inhalation	Fisher 344 rats	GD 6-15	**Doses:** 0.076, 0.23, and 0.45 mg/L for 6 hours per day **Replicates:** 32-37 per dose	**NOAEC:** 0.45 mg/L-day	**Methods:** • Test substance reported as CASRN 34590-94-8 • Purity 100% • EPA OTS 798.4350 • GLP compliant
5077934	Inhalation	Sprague Dawley rats	GD 6-15	**Doses:** 0, 0.1, 0.3, and 1.0 mg/L for 6 hours per day **Replicates:** 25 females per dose	**NOAEC:** 1.0 mg/L-day	**Methods:** • Test substance reported as CASRN 25498-49-1 • Purity 98.5% • GLP compliance not reported
5077932	Inhalation	Albino rats	GD 6-15	**Doses:** 0, 0.3, 0.9, 2.7, and 8.9 mg/L for 6 hours per day **Replicates:** 7 females per dose	**NOAEC:** 8.9 mg/L-day	**Methods:** • Test substance reported as CASRN 25498-49-1 • Purity 98.5% • GLP compliance not reported

Cancer		
Source	**Effect**	**Study Details**
Oncologic v8.0	OncoLogic currently has no assessment criteria regarding methyl esters and/or aliphatic ethers.	**Results:** • Structure could not be evaluated by Oncologic.
ISS v2.4[47]	Negative (Estimated) Tripropylene glycol butyl ether is a glycol ether which does not contain any structural features indicative of electrophilic potential.	**Methods:** • Carcinogenicity alerts (genotoxic and non-genotoxic) by ISS profiler as available within the OECD Toolbox v4.3 **Results:** • No alerts were identified for the parent structure (an aldehyde alert is flagged for its metabolite) (see Figure 10 metabolic tree in Metabolic Pathway Trees Supplemental Document[48]).

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

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

Table B.1: Human Health Hazard						
VEGA 1.1.4[49]	Tripropylene glycol butyl ether was processed through all 4 models. ISS 1.0.2 predicted it to be non-carcinogenic with moderate reliability.	**Methods:** • VEGA 1.1.4 contains 4 models for carcinogenicity – CAESAR 2.1.9, ISS 1.0.2, IRFMN/Antares 1.0.0, IRFMN/ISSCAN-GX 1.0.0 **Results:** • CAESAR 2.1.9: Low reliability (Tripropylene glycol butyl ether lies outside of the applicability domain (AD) of the model) • ISS 1.0.2: Moderate reliability (Tripropylene glycol butyl ether could lie outside of the AD) • IRFMN/Antares 1.0.0: Low reliability (Tripropylene glycol butyl ether lies outside of the AD) • IRFMN/ISSCAN-GX 1.0.0: Low reliability (Tripropylene glycol butyl ether lies outside of the AD)				
Genotoxicity						
Source	**Test Type & endpoint**	**Species & strain (if available)**	**Metabolic activation**	**Doses and controls**	**Results**	**Study Details**
5178583	Gene mutation (*in vitro*)	Salmonella typhimurium strains TA98, TA100, TA1535, and TA1537	With and without	**Doses:** 0, 50, 158, 500, 1580, and 5000 µg/plate	Negative	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity: 96.12% • OECD Guideline 471 • GLP compliant

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

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

Table B.1: Human Health Hazard						
5178578	Micronuclei assay (*in vivo*)	CD mice	NA	**Doses:** 0, 187.5, 625, and 1875 mg/kg bw	Negative	**Method:** • Test substance reported as CASRN 55934-93-5 • Purity 96.12% • OECD 474 • GLP compliant
5077927	Chromosomal aberrations (*in vitro*)	Rat liver RL4 cells	Without	**Doses:** 0, 625, 1250, 2500, and 5000 µg/mL	Negative	**Methods:** • Test substance reported as CASRN 34590-94-8 • Purity not reported • GLP compliance not reported
5077935	Chromosomal aberrations (*in vitro*)	CHL/IU cells	With and without	**Doses:** 0, 371, 741, and 1482 µg/mL	Negative	**Methods:** • Test substance reported as CASRN 34590-94-8 • Purity > 99% • Japan Guidelines for Screening Mutagenicity Testing of Chemicals • GLP compliant
5077938	DNA damage and repair	Rat hepatocyte cells	Without	**Doses:** 0.1, 0.316, 1, 3.16, 10, 31.6, and 100 mM	Negative	**Methods:** • Test substance reported as CASRN 25498-49-1 • Purity: 98.7% • GLP compliance not reported
5077989	Chromosomal aberrations (*in vitro*)	Chinese hamster ovary cells	With and without	**Doses:** 0, 101, 203, 405, 810, and 1620 µg/mL	Negative	**Methods:** • Test substance reported as CASRN 30025-38-8 • Purity not reported • OECD Guideline 473 • GLP compliant
4956637	Micronuclei assay (*in vivo*)	Mouse	With	**Doses:** 0, 250, 833, and 2500 mg/kg **Replicates:** 5 per sex per dose	Negative	**Methods:** • Test substance reported as CASRN 29911-28-2 • Purity: 99.5% • GLP compliant
4956637	Chromosomal aberrations (*in vitro*)	Chinese hamster ovary cells	With and without	**Doses:** • 0, 333, 1000, and 3332 µg/mL with metabolic activation;	Positive at cytotoxic concentrations (3332 µg/mL with activation)	**Methods:** • Test substance reported as CASRN 29911-28-2 • Purity > 95% • GLP compliant **Results:**

Table B.1: Human Health Hazard						
				• 0, 1000, 2000, 3000, and 4000 µg/mL without activation		• Cytotoxicity observed at 1000 and 3332 µg/mL with metabolic activation and 3000 and 4000 µg/mL without metabolic activation
4956637	Chromosomal aberrations (*in vitro*)	Chinese hamster ovary cells	With and without	**Doses:** • 0, 500, 1000, 2000, and 3000 µg/mL with metabolic activation • 0, 1000, 2000, 3500, and 5000 µg/mL without activation	Positive	**Methods:** • Test substance reported as CASRN 29911-28-2 • Purity not reported • GLP compliant **Results:** • Significantly increased frequency of aberrations was observed at 18-hour incubation period for 500, 1000 and 3000 µg/mL with metabolic activation and 1000 and 5000 µg/mL without metabolic activation • Cytotoxicity observed at 3000 µg/mL with metabolic activation and 5000 µg/mL without metabolic activation • But follow up in vivo test was negative
4956637	Chromosomal aberrations (*in vitro*)	Chinese hamster ovary cells	With and without	**Doses:** 0, 500, 1667, and 5000 µg/mL	Negative	**Methods:** • Test substance reported as CASRN 29911-28-2 • Purity: 99.5% • GLP compliant
Neurotoxicity						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
5077990	Oral (gavage)	CD-1 rats	90 days	**Doses:** 0, 50,225,1000 mg/kg-day **Replicates:** 10/sex/dose	**NOAEL**: 1000 mg/kg-day (males), 225mg/kg-day (females); **LOAEL**: 1000 mg/kg-day (females) based on effects on hindlimb grip strength	**Methods:** • Test substance reported as CASRN 30025-38-8 • Purity: >98% • OECD Guideline 408 • GLP compliant **Results:** • Neurological endpoints evaluated: brain, sciatic nerve and spinal cord histopathology; field and motor

Table B.1: Human Health Hazard						
						activity measurements; a battery of neurobehavioral functions that were not described. • No treatment effects on histopathology in brain, spinal cord and sciatic nerves or field or motor activity measurements. • The magnitude of effects to hindlimb grip strength in females were not reported. Hindlimb grip strength was not affected by treatment in males. • No effects were noted in males or females during 2-week recovery period.
4946620	Inhalation	Fisher 344 rats	13 weeks (6 hours/day, 5 days/week)	**Doses:** 0, 0.091, 0.393, or 1.212 mg/L **Replicates:** 10/sex/dose	**NOAEC**: 1.212 mg/L	**Methods:** • Test substance reported as CASRN 34590-94-8 • Purity: 99% • GLP compliance not reported. **Results:** • No effects on histopathology in the brain, peripheral nerve, or spinal cord.
4946620	Inhalation	New Zealand white rabbits	13 weeks (6 hours/day, 5 days/week)	**Doses:** 0, 0.091, 0.393, or 1.212 mg/L **Replicates:** 7/sex/dose	**NOAEC**: 1.212 mg/L	**Methods:** • Test substance reported as CASRN 34590-94-8 • Purity: 99% • GLP compliance not reported. **Results:** • No effects on histopathology in the brain, peripheral nerve, or spinal cord.
Irritation						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses**	**Effect**	**Study Details**
5178574	Dermal	New Zealand White rabbits	Exposure for 4 hours, observed for 7 days	**Dose:** 0.5 mL undiluted test substance **Replicates:** 3 rabbits	Moderately Irritating	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity: 99% • OECD Guideline 404 • GLP Compliant **Results:** • Slight erythema in 3/3 animals

Table B.1: Human Health Hazard						
						• Edema in 1/3 animals
5178579	Dermal	New Zealand White rabbits	Exposure for 4 hours, observed for 8 days	**Dose:** 0.5 mL undiluted test substance **Replicates:** 3 rabbits	Moderately Irritating	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity not reported • OECD Guideline 404 • GLP Compliant **Results:** • Slight erythema in 3/3 animals but fully reversible in 8 days
5178585	Ocular	New Zealand White rabbits	Single exposure, 14 day observation	**Dose:** 0.1 mL **Replicates:** 3 females	Moderately irritating	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity: 99% • OECD Guideline 405 • GLP compliance not reported **Results:** • Iris score: 0.3/2 at 24 hours but fully reversible by 48 hours • Conjunctivae score: 1.7/3 but fully reversible by 14 days • Chemosis score: 1/4 but fully reversible by 7 days
5178582	Ocular	New Zealand White rabbits	Single exposure, 72 hour observation	**Dose:** 0.1 mL of undiluted test substance **Replicates:** 3 total animals	Negative	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity not reported • OECD Guideline 405 • GLP compliant **Results:** **1 hour after exposure:** • Conjunctivae score: 2/3 • Chemosis score: 1.33/4 • Conjunctival discharge occurred in 3/3 animals **Averages for 24, 48 and 72 hours after exposure:** • Conjunctivae score: 0.3/3 • All other average scores were 0 • All effects fully reversible by 72 hours

Table B.1: Human Health Hazard						
Immunotoxicity						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
5178575	Oral (gavage)	Fischer 344 rats	28 days	**Doses:** 0, 100, 350 and 1000 mg/kg-day **Replicates:** 5 per sex per dose	**NOAEL:** 1000 mg/kg-day	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity: 80.67% • OECD Guideline 407 • GLP compliant **Results:** • High dose animals had increased platelet counts but they were in range with historical controls. • No treatment related changes in hematology, gross pathology and spleen weight
5178581	Oral (drinking water)	Fischer 344 rats	13 weeks	**Doses:** 0, 100, 350 and 1000 mg/kg-day **Replicates (by dose):** • 0 mg/kg-day: 20 per sex • 100 mg/kg-day: 10 per sex • 350 mg/kg-day: 10 per sex • 1000 mg/kg-day: 20 per sex	**NOAEL:** 1000 mg/kg-day	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity: 97.7% • OECD Guideline 408 • GLP compliant • 10/20 animals in the 0 mg/kg-day and 1000 mg/kg-day groups were given a 4-week recovery period **Results:** • No treatment related changes to lymphoid tissue weight or histology. • Decreased RBC counts, HGB concentrations, and HCT or PLAT counts were observed in males in the 1000 mg/kg bw-day dose group, however, these were not considered toxicologically or biologically significant due to the lack of corresponding histopathological changes and were within the range of values for historical controls.

Table B.1: Human Health Hazard						
3041622, 4944882	Dermal	Rabbits	90 days	**Doses:** 0, 950, 2850, 4750, and 9500 mg/kg-day **Replicates:** 5-7 males per group	**NOAEL:** 9500 mg/kg-day	**Methods:** • Test substance reported as CASRN 34590-94-8 • Purity not reported; test substance was presumably undiluted • Doses reported in mL/kg-day; converted to mg/kg-day based on a density of 0.95 g/mL • GLP compliance not reported **Results:** • No treatment related changes in hematology, gross pathology and organ weight related to lymphoid tissue.
4146480	Dermal	Porton-Wistar rats	28 days	**Doses:** 0, 100, and 1000 mg/kg-day **Replicates:** 8 males per group	**NOAEL:**1000 mg/kg-day	**Methods:** • Test substance reported as CASRN 34590-94-8 • Purity not reported • GLP compliance not reported **Results:** • No treatment related changes to clinical chemistry, hematology, or bone marrow.
5077871	Dermal	Rabbits	90 days	**Doses:** 0, 2850, and 4750 mg/kg-day **Replicates:** 5 males per group	**NOAEL:** 4750 mg/kg-day	**Methods:** • Test substance reported as CASRN 34590-94-8 • Purity not reported • GLP compliance not reported **Results:** • No treatment related changes in hematology or spleen weight.
4956637	Dermal	Wistar rats	13 weeks	**Doses:** 0, 91, 273, and 910 mg/kg-day **Replicates:** 10 per sex per group	**NOAEL:** 91 mg/kg-day **LOAEL:** 273 mg/kg-day based on increased white blood cell counts in both sexes	**Methods:** • Test substance reported as CASRN 29911-28-2 • Purity > 95% • GLP compliant **Results:** • Increased white blood cell (neutrophil) counts in the 273 and 910 mg/kg-day treatment group.

Table B.1: Human Health Hazard						
4944882, 5077872, 4956637	Dermal	Rabbits	90 days	**Doses:** 0, 960, 2900, 4,800, and 9600 mg/kg-day **Replicates:** 5-8 males per group	**NOAEL:** 9600 mg/kg-day	**Methods:** • Test substance reported as CASRN 25498-49-1 • Purity not reported • GLP compliance not reported **Results:** • No treatment related changes in hematology and lymphoid tissue.
4946620	Inhalation	Fisher 344 rats	13 weeks	**Doses:** 0, 0.091, 0.393, and 1.212 mg/L-day **Replicates:** 10 per sex per group	**NOAEC:** 1.212 mg/L-day	**Methods:** • Test substance reported as CASRN 34590-94-8 • Purity: 99% • GLP compliance not reported **Results:** • No treatment related changes to hematology, or lymphoid tissue.
4946620	Inhalation	New Zealand White rabbits	13 weeks	**Doses:** 0, 0.091, 0.393, and 1.212 mg/L-day **Replicates:** 10 per sex per group	**NOAEC:** 1.212 mg/L-day	**Methods:** • Test substance reported as CASRN 34590-94-8 • Purity: 99% • GLP compliance not reported **Results:** • No treatment related changes to hematology, or lymphoid tissue.

Table B.2: Environmental Hazard					
Aquatic Toxicity: Experimental					
Source	**Species & strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
4985128, 4985120	*Poecilia reticulata*	96 hours	**Doses:** 0, 56, 100, 180, 320, 560, and 1000 mg/L (nominal) **Replicates:** 2 replicates, each with 6 organisms per dose	**LC_{50}**: 564 mg/L (95% confidence 501 to 691 mg/L)	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity: 99% • OECD Guideline 203 • GLP compliant **Endpoints:** • Based on behavior (pigmentation, hyperactivity, and inhibition of swimming ability) • EC_{50} > 180 mg/L to < 320 mg/L • NOEC: 180 mg/L
4985123, 4985119	*Daphnia magna*	48 hours	**Doses:** 0, 12.5, 25, 50, 100 mg/L (nominal)	**EC_{50}** > 100 mg/L	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity not reported • OECD Guideline 202 • GLP compliant
4985112	*Pseudokirchneriella subcapitata*	5 days	**Doses:** 15.9, 22.3, 33.3, 50.7, 84.4, 135.2, 217.4, 355.4, 522.9 and 848.1 mg/L (measured)	**EC_{50}**: 351 mg/L (cell volume); 265 mg/L (cell count)	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity: 83% • EPA OPP 122-2 (Algal Toxicity, Tiers I and II) • GLP compliant
Aquatic Toxicity: Estimated					
Model	**Endpoint**	**Species**	**Predicted Effect Level**	**Notes**	
ECOSAR v2.0 (Class: Neutral Organics)	Chronic value	Freshwater fish	72 mg/L	SMILES Input: OCC(COCCOC(CCCOCC)C)C.	
ECOSAR v2.0 (Class: Neutral Organics)	Chronic value	Daphnia magna	35 mg/L	SMILES Input: OCC(COCCOC(CCCOCC)C)C.	
ECOSAR v2.0 (Class: Neutral Organics)	Chronic value	Green algae	56 mg/L	SMILES Input: OCC(COCCOC(CCCOCC)C)C.	

Table B.3: Fate					
Environmental Fate: Experimental					
Source	**Endpoint**	**Duration**	**Doses and number of replicates**	**Results**	**Study Details**
4951403, 4985135	Biodegradation	28 days	**Dose:** 90 mg/L	Readily biodegradable	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity: 97.7% • OECD Guideline 301F • GLP compliant **Results:** • Degradation during test: 10% in 7.3 days; 60% in 10.5 days; 72% at 10-day window; 59% in 28 days by O2 consumption; 58% average removal by DOC at 28 days and 56% mineralization to CO2 after 28 days
4985134	Biodegradation	14 days	**Doses:** 20 and 32 mg/L	Readily biodegradable	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity not reported • OECD Guideline 301A • GLP compliant **Results:** • Kinetic degradation results: 2% in 1 day, 9% in 3 days, 69% in 5 days, 88% in 7 days, and 96% in 14 days
4985143	Biodegradation	28 days	**Doses:** 10 and 20 mg/L	Not readily biodegradable	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity: 98.47% • OECD Guideline 301B • GLP compliant **Results:** • 21.5% and 24.3% in 28 days (for 10 and 20 mg/L, respectively), 32% and 31% in 37 days
4985140	Biodegradation	28 days	**Doses:** 141.7 and 139 mg DOC/L	Readily biodegradable	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity > 95% • OECD Guideline 302B • GLP compliant **Results:** • 86% in 14 days, 92% in 21 days, 93% in 28 days

Table B.3: Fate					
5077994	Anaerobic biodegradation	28 day	**Dose:** 51 mg/L DOC	Not anaerobically biodegradable	**Methods:** • Test substance identified as CASRN 34590-94-8 • Purity not reported • Test method equivalent to OECD 311 • GLP compliant • Digester sludge used as an innoculum **Results:** • Degradation results: 0% at 28 days, 10% at 42-81 days
4985126	Toxicity to microorganisms	30 minutes	**Doses:** 1000 mg/L (nominal)	Negative	**Methods:** • Test substance reported as CASRN 55934-93-5 • Purity not reported • OECD Guideline 209 • GLP compliant
Environmental Fate: Modelled					
Model	**Data Type**	**Endpoint**	**Predicted Endpoint**	**Notes**	
EPISuite v.4.11	Estimated	BAF	6.22	EPI Suite Physical Property Inputs - MP= -75 deg C; Log P = 1.896; WS = 25000 mg/L; HLC = 4.05E-08), SMILES: OC(C)COC(C)COC(C)COCCCC	
EPISuite v.4.11	Estimated	BCF	8.22 (regression on eq)		
EPISuite v.4.11 (BIOWIN 7)	Estimated	Anaerobic biodegradation	Not predicted to biodegrade quickly under anaerobic conditions	Predicted probability of -0.7805. Fragment representation is valid. Fast degradation is defined as predicted probability >0.5.	

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Rowe, VK; Mccollister, DD; Spencer, HC; Oyen, F; Hollingsworth, RL; Drill, VA. (1954). Toxicology of mono-, di-, and tri-propylene glycol methyl ethers. AMA Arch Ind Hyg Occup Med 9: 509-525.

Shell Chemical (Shell Chemical Company). (1983). Toxicity studies with Dowanol DPM: Tests for in vitro genotoxicity with attachments, cover sheets and letter dated 060689. (OTS0520390. EPA Doc No: 86-890000952). https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/OTS0520390.xhtml

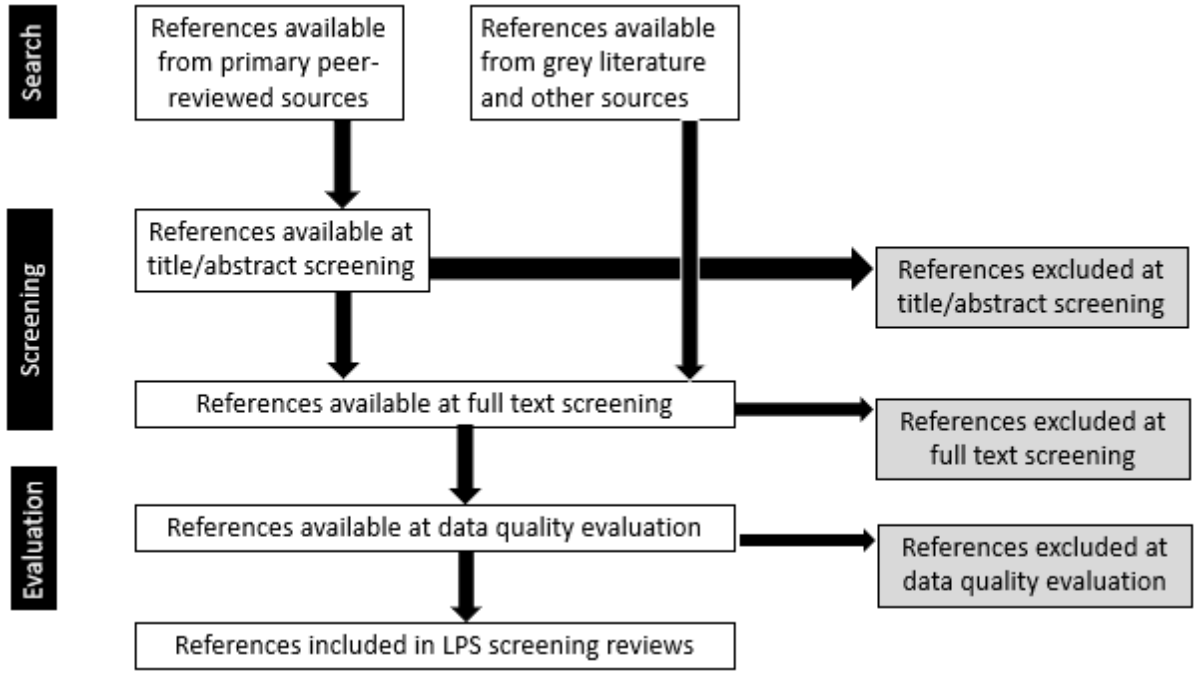
Appendix C: Literature Search Outcomes

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 tripropylene glycol n-butyl ether. Search outcomes and reference details are provided on the candidate's HERO[50] project page.

EPA created a fit-for-purpose process to transparently document the literature search and review[51] of available hazard and fate information for low-priority substance (LPS) candidates. References from peer-reviewed primary sources, grey sources,[52] 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, tripropylene glycol n-butyl ether, the following analogs were used for designation: dipropylene glycol, monoethyl ether (CASRN 30025-38-8);

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

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

[52] 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, methyl ether (CASRN 34590-94-8); dipropylene glycol, monobutyl ether (CASRN 29911-28-2); tripropylene glycol, monomethyl ether (25498-49-1). Dipropylene glycol, ethyl ether (15764-24-6) and tripropylene glycol, methyl ether (20324-33-8) were also considered. For more details and justification on analogs, see section 6.1.1. Analogs were used to fill data gaps on endpoints for which tripropylene glycol n-butyl ether lacked quality data, such as developmental toxicity, or to add to the weight of the scientific evidence. EPA collected reasonably available information for these endpoints by searching specific grey literature and other secondary sources, listed on Table C.1. If information related to the identified analogs were available in these sources, the references were screened and evaluated using the same process as references on tripropylene glycol n-butyl ether described above.[51] EPA also used read across from the LPS candidate, dipropylene glycol methyl ether acetate (CASRN 88917-22-0). The two LPS chemicals along with the analogs mentioned above fall under the propylene glycol ethers cluster in HERO.

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

C.1.2 Search Terms and Results

EPA began the literature review process for the hazard screening of tripropylene glycol n-butyl ether by developing search terms. To gather publicly available information, specific search terms were applied for each discipline and across databases and grey literature sources. Table C.2 lists the search terms used in the database search of peer-reviewed literature for the propylene glycol ethers cluster including tripropylene glycol n-butyl ether. For grey literature and other secondary sources, Table C.3 lists the search terms used for the propylene glycol ethers LPS candidates and analogs.

Table C.2: Search Terms Used in Peer Reviewed Databases		
Discipline	**Database**	**Search terms**[53]
Human Health	PubMed	88917-22-0[rn] OR 55934-93-5[rn] OR "dipropylene glycol monomethyl ether acetate"[nm] OR "((Butoxymethylethoxy)methylethoxy)propan-1-ol"[tw] OR "Dipropylene glycol monomethyl ether acetate"[tw] OR "Dowanol TPnB"[tw] OR "PPG-2 methyl ether acetate"[tw] OR "PPG-3 BUTYL ETHER"[tw] OR "Propanol, (2-(2-

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

Table C.2: Search Terms Used in Peer Reviewed Databases		
Discipline	**Database**	**Search terms**[53]
		butoxymethylethoxy)methylethoxy)-"[tw] OR "Propanol, (2-methoxymethylethoxy)-, acetate"[tw] OR "Propanol, 1(or 2)-(2-methoxymethylethoxy)-, acetate"[tw] OR "Tripropylene glycol butyl ether"[tw] OR "Tripropylene glycol n-butyl ether"[tw] OR "(2-(2-butoxymethylethoxy)methylethoxy)propanol"[tw] OR "(2-methoxymethylethoxy)propanol acetate"[tw]
	Toxline	(88917-22-0[rn] OR 55934-93-5[rn] OR "Dipropylene glycol monomethyl ether acetate" OR "PPG-2 methyl ether acetate") 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] "((Butoxymethylethoxy)methylethoxy)propan-1-ol" OR "Dowanol TPnB" OR "PPG-3 BUTYL ETHER" OR "Propanol, (2-(2-butoxymethylethoxy)methylethoxy)-" OR "Propanol, (2-methoxymethylethoxy)-, acetate" OR "Propanol, 1(or 2)-(2-methoxymethylethoxy)-, acetate" OR "Tripropylene glycol butyl ether" OR "Tripropylene glycol n-butyl ether" OR "(2-(2-butoxymethylethoxy)methylethoxy)propanol" OR "(2-methoxymethylethoxy)propanol acetate"
	TSCATS 1	(88917-22-0 [rn] OR 55934-93-5 [rn]) AND (TSCATS [org]) AND NOT PubMed [org] AND NOT pubdart [org]
	WOS	TS=("88917-22-0" OR "55934-93-5" OR "((Butoxymethylethoxy)methylethoxy)propan-1-ol" OR "Dipropylene glycol monomethyl ether acetate" OR "Dowanol TPnB" OR "PPG-2 methyl ether acetate" OR "PPG-3 BUTYL ETHER" OR "Propanol, (2-(2-butoxymethylethoxy)methylethoxy)-" OR "Propanol, (2-methoxymethylethoxy)-, acetate" OR "Propanol, 1(or 2)-(2-methoxymethylethoxy)-, acetate" OR "Tripropylene glycol butyl ether" OR "Tripropylene glycol n-butyl ether" OR "(2-(2-butoxymethylethoxy)methylethoxy)propanol" OR "(2-methoxymethylethoxy)propanol acetate") 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
	TSCATS 1	Same as human health strategy CASRN only
	Proquest	TITLE=("88917-22-0" OR "55934-93-5" OR "Butoxymethylethoxy methylethoxy propan-1-ol" OR "Dipropylene glycol monomethyl ether acetate" OR "PPG-2 methyl ether acetate" OR "Tripropylene glycol butyl ether" OR "Tripropylene glycol n-butyl ether") 2 hits manually added (+1 dupe within this query) SUBJECT=("88917-22-0" OR "55934-93-5" OR "Butoxymethylethoxy methylethoxy propan-1-ol" OR "Dipropylene glycol monomethyl ether acetate" OR "PPG-2 methyl ether acetate" OR "Tripropylene glycol butyl ether" OR "Tripropylene glycol n-butyl ether") 3 hits manually added

Table C.2: Search Terms Used in Peer Reviewed Databases		
Discipline	**Database**	**Search terms**[53]
		ABSTRACT=("88917-22-0" OR "55934-93-5" OR "Butoxymethylethoxy methylethoxy propan-1-ol" OR "Dipropylene glycol monomethyl ether acetate" OR "PPG-2 methyl ether acetate" OR "Tripropylene glycol butyl ether" OR "Tripropylene glycol n-butyl ether") "Dowanol TPnB" OR "PPG-3 BUTYL ETHER" OR "Propanol, 2- 2-butoxymethylethoxy methylethoxy -" OR "Propanol, 2-methoxymethylethoxy -, acetate" OR "2- 2-butoxymethylethoxy methylethoxy propanol" OR "2-methoxymethylethoxy propanol acetate"
Fate	WOS	Same as human health strategy synonyms only

Table C.3: Search terms used in grey literature and additional sources	
Chemical	**Search terms**
Propylene glycol ether cluster (Tripropylene glycol n-butyl ether; DPMA)	Query string searched as a string or individually depending on resource: "5131-66-8" OR "107-98-2" OR "108-65-6" OR "88917-22-0" OR "55934-93-5" OR "1-Butoxy-2-propanol" OR "1-methoxy 2-propyl acetate" OR "1-methoxy-2-propanol" OR "1-methoxy-2-propyl acetate" OR "1-Methoxypropan-2-ol" OR "2-acetoxy-1-methoxypropane" OR "2-methoxypropyl acetate" OR "2-methoxy-1-methylethyl acetate" OR "3-Methoxy-2-propanol" OR "Butoxypropanol" OR "Dipropylene glycol monomethyl ether acetate" OR "methoxyisopropanol" OR "Methoxyisopropyl acetate" OR "n-Butoxy-2-propanol" OR "PGMEA" OR "PPG-2 methyl ether acetate" OR "Propylene glycol methyl ether" OR "Propylene glycol monobutyl ether" OR "Propylene glycol monomethyl ether" OR "propylene glycol n-butyl ether" OR "1-Butoxypropan-2-ol" OR "1-methoxy-2-acetoxypropane" OR "propylene glycol 1-methyl ether" OR "Propyleneglycol monomethyl ether acetate" OR "Tripropylene glycol butyl ether" OR "Tripropylene glycol n-butyl ether"
Analogs searched	Dipropylene glycol, ethyl ether (15764-24-6); dipropylene glycol, monoethyl ether (30025-38-8); dipropylene glycol, methyl ether (34590-94-8); dipropylene glycol, monobutyl ether (29911-28-2); tripropylene glycol, monomethyl ether (25498-49-1); tripropylene glycol, methyl ether (20324-33-8)

After the search terms were applied, more than 100 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.[51] Of these, 48 references were included for data evaluation and used to support the designation of tripropylene glycol n-butyl ether 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 tripropylene glycol n-butyl ether. 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[51] 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 tripropylene glycol n-butyl ether, EPA excluded a total of 47 references when assessing human health hazard. Off-topic references (e.g., studies that did not contain information relevant to human health) were excluded at either title/abstract screening (see Table C.4), or full-text screening (see Table C.5). Unacceptable references (e.g., studies that did not meet data quality metrics) were excluded at full-text screening (see Tables C.6 and C.7). Off-topic and unacceptable references are displayed next to the corresponding exclusion criteria.

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

Reference excluded (HERO ID) because the reference did NOT contain information needs[54] relevant to human health hazard									
1549118	4742957	2292715	4951403						
Reference excluded (HERO ID) because the reference primarily contained *in silico* data									
4946621									

Table C.5: Screening Questions and Off-Topic References Excluded at Full Text Screening for Human Health Hazard

Question	Off-topic if answer is:	References excluded (HERO ID)
Does the reference contain information pertaining to a low- priority substance candidate?	No	58939 95230 655409 3114932 5015980 5015981 5015982

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

Table C.5: Screening Questions and Off-Topic References Excluded at Full Text Screening for Human Health Hazard		
Question	**Off-topic if answer is:**	**References excluded (HERO ID)**
		5015983 5015985 5015986 5015987 5015988 5015989 5015990 5015992 5015993 5015994 5015996 5015997 5015998 5015999 5016000 5016001 5016002 5016003 5016004 5016005 5016006 5016009 5016011 5016015 5016016 5016020 5015992 5015994
What type of source is this reference?	Review article or book chapter that contains only citations to primary literature sources	4851358 5015978
What kind of evidence does this reference primarily contain?	*In silico* studies that DO NOT contain experimental verification	N/A.

Table C.5: Screening Questions and Off-Topic References Excluded at Full Text Screening for Human Health Hazard		
Question	**Off-topic if answer is:**	**References excluded (HERO ID)**
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	3114932
The following question apply to ANIMAL evidence only		
Does the reference report an exposure route that is by inhalation, oral, or dermal route?	No	5015178
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	5015178
Does the reference report an exposure to the test substance only (i.e. no mixtures with the exception of aqueous solutions and reasonable impurities and byproducts)?	No	N/A.
Does the paper report a negative control that is a vehicle control or no treatment control?	No[55]	5015178
The following questions apply to MREPORTED TO THE MECHANISTIC/ALTERNATIVE TEST METHODS evidence only		
Does the reference report a negative control that is a vehicle control or no treatment control?	No	N/A.

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

Table C.5: 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	N/A.

Table C.6: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Human Health Hazard – Animal		
Data Quality Metric	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 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.	4956637
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).	4956637
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).	2530089 4956637 5016012

Table C.6: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Human Health Hazard – Animal		
Data Quality Metric	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 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).	2530089
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).	5015171 2530089 5015991
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).	2530089 4956637 5015171 5015991
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.).	2530089 4956637 5015171 5015991
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.	2530089 4956637 5014494

Table C.7: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Human Health Hazard – In Vitro		
Data Quality Metric	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 1: Test substance identity	The test substance identity or description cannot be determined from the information provided (e.g., nomenclature was unclear and CASRN or structure were not reported). **OR** For mixtures, the components and ratios were not characterized or did not include information that could result in a reasonable approximation of components.	4956637
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).	4956637
Metric 5: Reporting of concentration	The exposure doses/concentrations or amounts of test substance were not reported.	N/A.
Metric 6: Exposure duration	No information on exposure duration(s) was reported. **OR** The exposure duration was not appropriate for the study type and/or outcome of interest (e.g., 24 hours exposure for bacterial reverse mutation test).	2530089
Metric 7: Metabolic activation	No information on the characterization and use of a metabolic activation system was reported. **OR**	N/A.

Table C.7: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Human Health Hazard – In Vitro		
Data Quality Metric	**Unacceptable if:**	**References excluded (HERO ID)**
	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 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).	4956637

C.2.2 Environmental Hazard

For the screening review of LPS candidate tripropylene glycol n-butyl ether, EPA excluded a total of 21 references when assessing environmental hazard. Off-topic environmental hazard references excluded at title/abstract screening are listed in Table C.8, and those excluded at full-text screening are listed in Table C.9. References in Table C.10 represent unacceptable studies based on specific data quality metrics for environmental hazard. Off-topic and unacceptable references are displayed next to the corresponding exclusion criteria.

Table C.8: Off-Topic References Excluded at Title/Abstract Screening for Environmental Hazard									
Reference excluded (HERO ID) because the reference did NOT contain information needs[56] relevant to environmental hazard									
4742957	2563138	2530089	2292715	1549118	44187	3114932	4951403	4946621	3114932
4946621	4742957								
Reference excluded (HERO ID) because the reference did NOT present quantitative environmental hazard data									
N/A.									

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

Table C.9: Screening Questions and Off-Topic References Excluded at Full Text Screening for Environmental Hazard		
Question	**Off-topic if answer is:**	**References excluded (HERO ID)**
Does the reference contain information pertaining to a low- priority substance candidate?	No	3827368 4985113 4985115 4985117 4985121 4985125 4985127 4985130 4985131 4985132
What type of source is this reference?	Review article or book chapter that contains only citations to primary literature sources	N/A.
Is quantitative environmental hazard data presented?	No	N/A.
Is this primarily a modeling/simulation study? [Note: select "No" if experimental verification was included in the study]	Yes	N/A.
Is environmental hazard data presented for standard or non-standard aquatic or terrestrial species (fish, invertebrates, microorganisms, non-mammalian terrestrial species)?	No	N/A.
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	4985113 4985116 4985125 4985130
Does the reference include endpoints in the information needs?	No	N/A.

Table C.10: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Environmental Hazard		
Question	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 1: Test substance identity	The test substance identity or description cannot be determined from the information provided (e.g., nomenclature was unclear, CASRN or structure were not reported, substance name/ description does not match CASRN). **OR** For mixtures, the components and ratios were not characterized or did not include information that could result in a reasonable approximation of components.	4956637
Metric 2: Negative controls	A concurrent negative control group was not included or reported.	N/A.
Metric 3: Experimental system	The experimental system (e.g., static, semi-static, or flow-through regime) was not described.	N/A.
Metric 4: Reporting of concentrations	Test concentrations were not reported.	N/A.
Metric 5: Exposure duration	The duration of exposure was not reported. **OR** The reported exposure duration was not suited to the study type and/or outcome(s) of interest (e.g., study intended to assess effects on reproduction did not expose organisms for an acceptable period of time prior to mating).	N/A.
Metric 6: Test organism characteristics	The test species was not reported. **OR** The test species, life stage, or age was not appropriate for the outcome(s) of interest.	N/A.
Metric 7: Outcome assessment methodology	The outcome assessment methodology was not reported.	N/A.
Metric 8: Reporting of data	Data presentation was inadequate. **OR** Major inconsistencies were present in reporting of results.	N/A.

C.2.3 Fate

For the screening review of LPS candidate tripropylene glycol n-butyl ether, EPA excluded a total of 9 references when assessing environmental fate. Off-topic fate references excluded at title/abstract screening are listed in Table C.11, and those excluded at full-text screening are listed in Table C.12. References in Table C.13 represent unacceptable studies based on specific data quality metrics for fate. Off-topic and unacceptable references are displayed next to the corresponding exclusion criteria.

Table C.11: Off-Topic References Excluded at Initial Screening for Fate									
Reference excluded (HERO ID) because the reference did NOT contain information needs[57] relevant to environmental fate									
1549118	2292715	2530089	4946621	4742957					
Reference excluded (HERO ID) because the reference did NOT present quantitative environmental fate data									
N/A.									

Table C.12: Screening Questions and Off-Topic References Excluded at Full Text Screening for Fate		
Question	**Off-topic if answer is:**	**References excluded (HERO ID)**
Does the reference contain information pertaining to a low- priority substance candidate?	No	4985137 4985138 4985141
What type of source is this reference?	Review article or book chapter that contains only citations to primary literature sources	N/A.
Is quantitative fate data presented?	No	N/A.
Is this primarily a modeling/simulation study? [Note: Select "Yes" only if there is no experimental verification]	Yes	N/A.

Table C.13: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Fate		
Data quality metric	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 1: Test substance identity	The test substance identity or description cannot be determined from the information provided (e.g., nomenclature was unclear and CASRN or structure were not reported). **OR**	N/A.

[57] 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.13: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Fate		
Data quality metric	**Unacceptable if:**	**References excluded (HERO ID)**
	For mixtures, the components and ratios were not characterized or did not include information that could result in a reasonable approximation of components.	
Metric 2: Study controls	The study did not include or report crucial control groups that consequently made the study unusable (e.g., no positive control for a biodegradation study reporting 0% removal). **OR** The vehicle used in the study was likely to unduly influence the study results.	4956637
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.	4956637
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.	4956637
Metric 5: Testing conditions	Testing conditions were not reported, and the omission would likely have a substantial impact on study results. **OR** Testing conditions were not appropriate for the method (e.g., a biodegradation study at temperatures that inhibit the microorganisms).	N/A.
Metric 6: System type and design- partitioning	Equilibrium was not established or reported, preventing meaningful interpretation of study results.	N/A.

Table C.13: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Fate		
Data quality metric	**Unacceptable if:**	**References excluded (HERO ID)**
	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.	
Metric 7: Test organism-degradation	The test organism, species, or inoculum source were not reported, preventing meaningful interpretation of the study results.	4956637
Metric 8: Test organism-partitioning	The test organism information was not reported. **OR** The test organism is not routinely used and would likely prevent meaningful interpretation of the study results.	N/A.
Metric 9: Outcome assessment methodology	The assessment methodology did not address or report the outcome(s) of interest.	N/A.
Metric 10: Data reporting	Insufficient data were reported to evaluate the outcome of interest or to reasonably infer an outcome of interest. **OR** The analytical method used was not suitable for detection or quantification of the test substance. **OR** 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.	4956637
Metric 12: Verification or plausibility of results	Reported value was completely inconsistent with reference substance data, related physical chemical properties, or otherwise implausible, indicating that a serious study deficiency exists (identified or not).	N/A.

Appendix D: Summary of Public Comments

On March 21, 2019, EPA initiated the prioritization process for 20 chemical substances as candidates for designation as Low-Priority Substances. EPA published a document in the Federal Register providing the identity of the chemical substances being initiated for prioritization and a general explanation of why the Agency chose these chemical substances. EPA provided a 90-day comment period during which interested persons could submit relevant information on these chemical substances.[58]

For tripropylene glycol n-butyl ether, EPA received public comment recommending that the Agency consider specific publicly available data sources. EPA reviewed all of these sources as part of its screening review of the chemical. Table 1 below lists these recommended sources, the HERO ID (if applicable), and notes about each source. EPA used the Health & Environmental Research Online (HERO) database to search, retrieve, and/or store data sources supporting scientific assessments. For references with HERO IDs, more information on the references can be found by searching the HERO ID at https://hero.epa.gov/hero/index.cfm/search/index.

Table D.1: Recommended Sources for Tripropylene Glycol N-Butyl Ether based on Public Comment

Source	HERO ID	Notes
Amended Safety Assessment of Butyl Polyoxyalkylene Ethers as Used in Cosmetics	2530089	This assessment was part of EPA's literature review process but was excluded due to data quality issues.

[58] Docket number EPA-HQ-OPPT-2019-0131 includes the list of 20 chemical substances that are candidates for designation as Low-Priority Substances for risk evaluation (https://www.federalregister.gov/documents/2019/03/21/2019-05404/initiation-of-prioritization-under-the-toxic-substances-control-act-tsca). Individual dockets were established for each of the 20 low-priority candidates. Docket number EPA-HQ-OPPT-2019-0118 addresses tripropylene glycol n-butyl ether.