Supporting Information for Low-Priority Substance Propanol, 1(or 2)-(2-Methoxymethylethoxy)-, Acetate (CASRN 88917-22-0) (DPMA)

Final Designation

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1. Introduction

The Lautenberg amendments to the Toxic Substances Control Act (TSCA) require EPA to designate chemical substances as either High-Priority Substances for risk evaluation, or Low-Priority Substances for which risk evaluations are not warranted at this time (section 6(b)(1)(B) and implementing regulations (40 CFR 702.3)). A high-priority substance is defined as a chemical substance that the Administrator concludes, without consideration of costs or other non-risk factors, may present an unreasonable risk of injury to health or the environment because of a potential hazard and a potential route of exposure under the conditions of use, including an unreasonable risk to potentially exposed or susceptible subpopulations identified as relevant by the Administrator. If the Administrator concludes, based on information sufficient to establish, without consideration of costs or other non-risk factors, that the high-priority standard is not met, then the substance must be designated as a low-priority substance. Propanol, 1(or 2)-(2-methoxymethylethoxy)-, acetate, referenced as DPMA 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 DPMA 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.

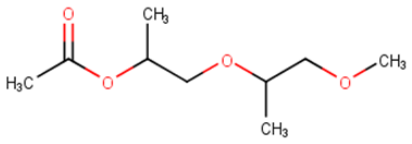
- *Appendix B (Hazard Characterization):* This appendix contains information on each of the studies used to support the hazard evaluation of the chemical substance.

- *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 Dipropylene Glycol Methyl Ether Acetate

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

Table 1: DPMA at a Glance	
Chemical Name	Dipropylene Glycol Methyl Ether Acetate
CASRN	88917-22-0
Synonyms	DPMA; 1-(3-Methoxypropoxy)propyl acetate; Glycol Ether DPM Acetate; 1(or2)-(2-methoxymethylethoxy)-propanoacetate; propanol,1(or2)-(2-methoxymethylethoxy)-,acetate; PPG-2 Methyl Ether Acetate
Trade Name(s)	DPMAc; Dowanol DPMA
Molecular Formula	$C_9H_{18}O_4$
Representative Structure	
Source(s): Kim et al. (2016); DeLima Associates (2018); Dow (2015)	

DPMA is a propylene oxide-based, or P-series, glycol ether acetate. DPMA is an organic chemical compound that contains an ester functional group comprised of two alkyl groups connected by a carbonyl and a linking oxygen atom (RCOOR') and two ether functional groups--an oxygen atom connected two alkyl groups (R-O-R'). DPMA is commercially produced as a mixture of four isomeric components in which the internal ether linkage may be adjacent to either a primary or secondary carbon atom. Shorter chain ethers and esters, such as DPMA, are liquids capable of dissolving other substances and typically function as solvents. DPMA is a colorless, water-soluble, sweet-smelling liquid with a moderate evaporation rate, and it is miscible with organic solvents. These properties make DPMA useful as a solvent, fragrance, film-forming agent, and coalescing 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 DPMA. 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 DPMA

Source/ Model	Data Type	Endpoint	Endpoint value	Notes
Sigma Aldrich 2019	Experimental	Physical state at room temp (based on melting point)	Liquid	
Staples and Davis 2002, OECD SIDS 2003 (SIDS)	Experimental	Molecular weight	190 g/mol	
EPISuite v.4.11[4]	Calculated	Molecular weight	190.2 g/mol	
Lyman 1990	Experimental	Molar volume	230.9 cm^3/mol	
Staples and Davies 2002; OECD SIDS 2003	Experimental	Water solubility	$1.60x10^5$ mg/L	
Reported to the ECHA database, 2019	Experimental	Water solubility	183000 mg/L at 20°C and pH 4.34; 160000 mg/L	
ChemIDPlus 2019	Experimental	Water solubility	194000 mg/L at 25°C	
EPISuite v.4.11	Estimated	Water solubility	40450 mg/L (calculated from log K_{ow}); 173000 mg/L (calculated by fragment)	
Staples and Davis 2002; OECD SIDS 2003	Experimental	Water solubility	0.841 mol/L	
Reported to the ECHA database, 2019	Experimental	Water solubility	0.926 mol/L	
ChemIDPlus 2019	Experimental	Water solubility	1.02 mol/L	

[4] EPI Suite Physical Property Inputs – Melting Point = -25.2 deg C, Boiling Point = 200 deg C, Vapor Pressure = 0.13 mm Hg, Water Solubility = 194000 mg/L, Log K_{ow} = 0.803, Henry's Law 2.0E-07 atm-m3/mole, SMILES: CC(=O)OC(C)COC(C)COC

Table 2: Physical-Chemical Properties for DPMA				
Source/ Model	**Data Type**	**Endpoint**	**Endpoint value**	**Notes**
Staples and Davis 2002; OECD SIDS 2003	Experimental	Log K_{ow}	0.803	
Reported to the ECHA database, 2019	Experimental	Log K_{ow}	0.61	
EPISuite v.4.11	Estimated	Log K_{ow}	0.66	
EPISuite v.4.11	Estimated	Log K_{oa}	5.89	
EPISuite v.4.11	Estimated	Log K_{oc}	1 (MCI); 1.12 (K_{ow})	
Staples and Davis 2002	Experimental	Vapor pressure	0.13 mm Hg (17 Pa)	
Reported to the ECHA database, 2019	Experimental	Vapor pressure	$7.80x10^{-2}$ mm Hg (10.4 Pa at 20°C); 1.93 mm Hg (2.57 mbar) at 20°C; 0.13 mm Hg (17 Pa)	
OECD SIDS 2003	Experimental	Vapor pressure	0.13 mm Hg at 25°C (17 Pa); <1 mm Hg at 20°C; 0.0836 mm Hg at 20°C	
EPISuite v.4.11	Estimated	Vapor pressure	$3.60x10^{-1}$ mm Hg	
EPISuite v.4.11	Estimated	Henry's Law	2.0E-07 atm-m^3/mol	
Staples and Davis 2002	Experimental	Henry's Law	2.0E-07 (0.02 Pa-m3/mole)	
EPISuite v.4.11	Estimated	Volatilization	168 days (river) 1841 days (lake)	
EPISuite v.4.11	Estimated	Photolysis (Indirect)	3.82 hours ($T_{1/2}$)	• OH rate constant 3.36 E-11 cm^3/molecule-second (12 hour day; 1.5E6 OH/cm^3) • No ozone reaction estimation
EPISuite v.4.11	Estimated	Hydrolysis	K_b half-life 88 days at pH 8; 2.4 years at pH 7	
EPISuite v.4.11	Estimated	Biodegradation potential	Ready prediction: No	
EPISuite v.4.11	Estimated	Wastewater treatment plant removal	94% Total Removal (92% biodegradation, 0.28% sludge, 0.9% air)	Input parameters: BIOP = 4, BioA = 1 and BioS = 1 based on 58% and 84% degraded after 28 days in a 301D test
EPISuite v.4.11	Estimated	BAF	1.1	
EPISuite v.4.11	Estimated	BCF	3.2	

Based on its reported physical form and measured melting point, DPMA is a liquid under ambient conditions (Sigma Aldrich, 2019). Liquids have the potential for exposure via direct dermal contact with the substance, ingestion and 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 measured vapor pressure, DPMA is expected to be volatile when in neat form at ambient temperatures. As a result, exposure to DPMA is possible through inhalation of vapors or aerosols if they are generated. Based on measured solubility data, DPMA is considered water soluble, indicating the potential for this substance to dissolve in water and form an aqueous solution (Reported to the ECHA database, 2019). 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 DPMA is present in diluted form. The estimated Henry's Law constant (Reported to the ECHA database, 2019; EPI Suite, 2019) for DPMA indicates 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}, absorption and sequestration in fatty tissues are unlikely, as reflected in the estimated BCF and BAF values for this compound (EPI Suite, 2019). The estimated log K_{oc} indicates this substance is highly mobile in soils, increasing its potential for leaching into and transport in groundwater, including ground water sources of drinking water (EPI Suite, 2019). If oral exposure occurs via ingestion of contaminated drinking water, including well water, absorption through the gastrointestinal tract is expected to be moderate based on the log K_{ow} (EPI Suite, 2019). Concern for presence in drinking water is reduced in part by DPMA's expected low persistence. Experimental biodegradation data indicate this substance is inherently biodegradable, meaning that it has the potential to break down in the environment into carbon dioxide and water (Reported to the ECHA database, 1996, 4985142).

3.1 References

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Sigma Aldrich (2019). Di(propylene glycol) methyl ether acetate, mixture of isomers. Retrieved from https://www.sigmaaldrich.com/catalog/product/aldrich/406562?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

4. Relevant Assessment History

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

To better understand the hazard and exposure profile of certain chemical substances, the Preliminary Assessment Information Rule (PAIR) under TSCA required manufacturers and importers to submit a standardized reporting form for each site at which they were manufacturing or importing a listed chemical. The chemical substances chosen for this rule were those with possibly high exposure potential or for which information about toxicity had been previously obtained. Also relevant to the listing decision: 1) whether other Federal agencies had identified the chemical or mixture as potentially posing a health risk, 2) the chemical's potentially high toxicity, 3) the chemical's high production volumes, or 4) the lack of completed preliminary assessments for the chemical. Inclusion of DPMA in the 1993 PAIR rule is not a concern because of EPA's high confidence in the chemical's low hazard profile.

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

The OECD Screening Information Datasets (SIDS) Initial Assessment Meeting (SIAM) discussed the SIDS Initial Assessment Report (SIAR) on propylene glycol ethers, including DPMA, in November 2003. The SIAM determined this chemical to be "low priority for further work" for human health and the environment.[7]

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

The German Environment Agency (UBA) designated DPMA as "low hazard to waters" in August 2017 based on an assessment of ecotoxicity and environmental fate.[9]

[5] https://www.epa.gov/saferchoice/safer-ingredients
[6] https://www.epa.gov/sites/production/files/2013-12/documents/dfe_master_criteria_safer_ingredients_v2_1.pdf
[7] https://hpvchemicals.oecd.org/ui/handler.axd?id=fdbb6972-3dd4-4046-ba21-eeb6e28c05fb
[8] https://www.ec.gc.ca/ese-ees/default.asp?lang=En&n=9F0069F1-1
[9] https://webrigoletto.uba.de/rigoletto/public/searchDetail.do?kennummer=8237

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 DPMA (Appendix A) to inform which uses would be determined conditions of use.[10] One source of information that EPA used to help determine conditions of use is 2016 Chemical Data Reporting (CDR). The CDR rule (previously known as the Inventory Update Rule, or IUR), under TSCA section 8, requires manufacturers (including importers) to report information on the chemical substances they produce domestically or import into the U.S., generally above a reporting threshold of 25,000 lb. per site per year. CDR includes information on the manufacturing, processing, and use of chemical substances with information dating to the mid-1980s. CDR may not provide information on other life-cycle phases such as the chemical substance's end-of-life after use in products (i.e., disposal).

According to CDR, DPMA is manufactured domestically and imported. It is used in processing (incorporation into formulation, mixture or reaction) for printing ink manufacturing, cleaning compound and toilet preparation manufacturing, and paint and coating manufacturing; it is also used as a reactant in wholesale and retail trade, and paint and coating manufacturing. Examples of industrial, commercial, and consumer uses include ink, toner, and colorant products, paints and coatings, and lubricants and greases. Based on the known manufacturing, processing, and uses of this chemical substance, EPA assumes distribution in commerce. According to CDR, DPMA was recycled by at least one facility. No information on disposal is found in CDR or through EPA's Toxics Release Inventory (TRI) Program[11] because DPMA is not a TRI-reportable chemical. Although reasonably available information did not specify additional types of disposal, for purposes of this prioritization designation, EPA assumed end-of-life pathways that include releases to air, wastewater, surface water, and land via solid and liquid waste based on the conditions of use (e.g., incineration, landfill).

To supplement CDR, EPA conducted research through the publicly available databases listed in Appendix A (Table A.2) and performed additional internet searches to clarify conditions of use or find additional occupational[12] and consumer uses. This research improved the Agency's understanding of the conditions of use for DPMA. Although EPA identified uses of DPMA 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 DPMA 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).

[10] 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).

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

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

Table 3: Conditions of Use for DPMA			
Life Cycle Stage	**Category**	**Subcategory of Use**	**Source**
Manufacturing	Domestic manufacture	Domestic manufacture	EPA (2017b)
	Import	Import	
Processing	Processing- incorporation into formulation, mixture or reaction	Solvents (which become part of product formulation or mixture) – printing ink manufacturing, soap, cleaning compound, and toilet preparation manufacturing, paint and coating manufacturing,	EPA (2017b)
		Solvents (for cleaning and degreasing) - soap, cleaning compound, and toilet preparation manufacturing	
		Odor agents – fragrances; soap, cleaning compound, and toilet preparation manufacturing	
	Processing as a reactant	Solvents (which become part of product formulation or mixture) - wholesale and retail trade, paint and coating manufacturing	
	Transportation equipment manufacturing	Trade and repair of motor vehicles and motorcycles	SPIN (2018)
	Chemical manufacturing		SPIN (2018)
	Manufacture of rubber and plastic products	Auto and tire care, tire protectant	SPIN (2018); NLM (2018b); Meguiars Inc. (2008); CPCat (2019)
	Recycling	Recycling	EPA (2017b)[13]
Industrial	Paint and coating manufacturing	Solvents (which become part of product formulation or mixture)	EPA (2017b)
Distribution	Distribution	Distribution	EPA (2017b)
Industrial/Commercial uses	Fuels and related products		Synapse Information Resources (n.d.)

[13] In the 2016 CDR, one facility (CBI) reported that DPMA was recycled (recycled, remanufactured, reprocessed, or reused). Nineteen facilities reported that DPMA was not recycled, while eight facilities withheld this information and three reported it as CBI.

Table 3: Conditions of Use for DPMA			
Industrial/commercial/ consumer uses	Ink, toner, and colorant products	Photochemical and reprographic agents, printing and reproduction of recorded media, Screen wash	EPA (2017b); SPIN (2018); Chemical Consultants Inc. (2018)
	Paints and coatings	Coatings and paints; screen printing and roll coating	EPA (2017b); Monument Chemical (2018); Synapse Information Resources (n.d.); NLM (2018a); Reported to the ECHA database, 2018; Dow (2015); SPIN (2018)
	Electronics		Synapse Information Resources (n.d.)
	Lubricants and greases	Lubricants, greases, release products	Reported to the ECHA database, 2018
	Mining		Synapse Information Resources (n.d.)
	Metal products not covered elsewhere	Welding and soldering products	Reported to the ECHA database, 2018
Commercial/consumer	Cleaning and furnishing care products	Penetrating solvent/lubricant, floor polishes	EPA (2017b); DeLima Associates (2014); CPCat (2019); Monument Chemical (2018); Synapse Information Resources (n.d.)
	Laundry and dishwashing products		EPA (2017b)
	Adhesives and sealants		Synapse Information Resources (n.d.); Reported to the ECHA database, 2018
Consumer	Air Care Products		EPA (2017b); DeLima Associates (2015); CPCat (2019); Reported to the ECHA database, 2018
	Anti-freeze and de-icing products		Reported to the ECHA database, 2018
	Surface treatment		Synapse Information Resources (n.d.); Reported to the ECHA database, 2018
	Textiles		Reported to the ECHA database, 2018
Disposal	Releases to air, wastewater, solid and liquid wastes.		Though not explicitly identified, releases from disposal were assumed to be reasonably foreseen[14]

[14] 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[15] 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 DPMA against the endpoints listed below. EPA's New Chemicals Program has used these endpoints for decades to evaluate chemical substances under TSCA[16] 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[17] 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[18]	**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

[15] 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.

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

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

[18] 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)[19]		**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[20]		**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[21]	**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.		

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

[20] 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).

[21] 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[22]	**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[23] evidence in humans)	Negative studies or robust mechanism-based SAR
Sensitization[24]		**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[25]	**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

[22] 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).

[23] 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.

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

[25] 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)[26]	**Chronic Aquatic Toxicity Value (L/E/IC50)**[26]	**Persistence (Measured in terms of level of biodegradation)**[27]	**Bioaccumulation Potential**[28]
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

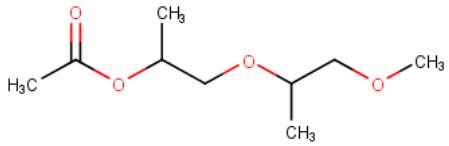
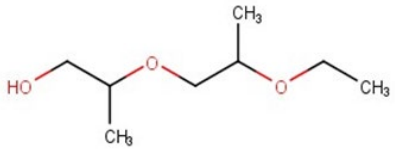
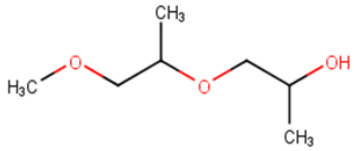
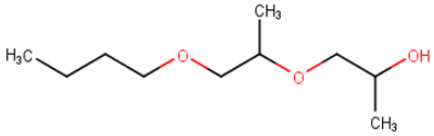
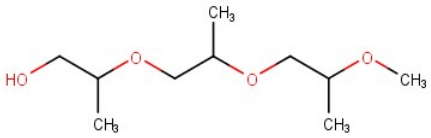
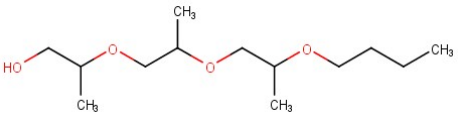
Below is a summary of the reasonably available information that EPA included in the hazard evaluation of DPMA. In many cases, EPA used analogous chemicals to make findings for a given endpoint. Where this is the case, use of the analog is explained. If the chemical studied is not named, the study is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

DPMA is an acetic acid ester of a propylene glycol ether composed of two methylethoxy repeating units with a methyl ether substitution on one of the terminal alcohols. It is a mixture of positional isomers, in which the positions of the methyl groups are variable. EPA used best professional judgement to select analogs for DPMA 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 of the analogs presented in Table 5 are either di- or tri-propylene glycol ethers that vary by the length of the aliphatic ether chain length (methyl, ethyl, or butyl). Analogs are expected to metabolize via similar pathways *in vivo*. The ester group in the target chemical is expected to rapidly hydrolyze *in vivo* to the corresponding propylene glycol ether. Four of the analogs are isomeric mixtures that may contain either the 1-methylethyl or 2-methylethyl substitution patterns in each propylene glycol unit. However, 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 DPMA.

[26] 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).*

[27] 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)*.

[28] 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: DPMA and Analog Structures		
CASRN	**Name**	**Structure**
88917-22-0	Dipropylene glycol methyl ether acetate (DPMA) (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
55934-93-5	Tripropylene glycol n-butyl ether (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[29] were only identified for the CASRNs listed in Table 5.

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

6.1.1 Absorption, Distribution, Metabolism, and Excretion

To review absorption, distribution, metabolism and excretion (ADME) endpoints without adequate quality[29] 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 DPMA's molecular weight and water solubility (Section 3), the potential for absorption through the lungs from inhalation exposure is likely. If oral ingestion occurs, absorption though the gastrointestinal tract is expected to be moderate. Due to its log K_{ow} (Section 3), dermal absorption is expected to be poor to moderate.

Distribution

Because DPMA is water soluble, 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[30] on DPMA's metabolite formation were not reasonably available for the assessment of metabolism. The Quantitative Structure-Activity Relationship (QSAR) toolbox[31] 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 DPMA metabolites. All three models predicted 1-(2-methoxy-1-methylethoxy)propan-2-ol, 3-(3-methoxypropoxy)-1-Propanol, 1-(3-methoxypropoxy)propan-1-ol and acetic acid as metabolites of DPMA. Additional metabolites of DPMA identified by one or more of the metabolism simulators included derivative esters, primary and secondary alcohols, carboxylic acids, aldehydes, ketones and secondary diols.

Excretion

Based on DPMA's physical-chemical properties (Section 3), it is expected that following exposure, DPMA will be primarily excreted in the urine or exhaled as CO_2. A minimal amount is expected to be excreted in feces.

6.1.2 Acute Toxicity

EPA assessed the potential for mammalian toxicity from acute exposure to DPMA using results from oral, dermal, and inhalation exposure studies.

A study on rats dosed with a single exposure of DPMA by oral gavage indicated a LD_{50} of 5448 mg/kg in females and an LD_{50} greater than 5000 mg/kg in males (Robinson et al., 2009; OECD, 2003; Reported to the ECHA database, 1982c). In another study, there were no mortalities in rats dosed with 5000 mg/kg DPMA via oral gavage (Reported to the ECHA database, 1990d). These results provide

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

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

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

A study on rabbits exposed to DPMA dermally reported no adverse effects at the single dose tested (5000 mg/kg), resulting in an LD_{50} greater than 5000 mg/kg (OECD, 2003; Reported to the ECHA database, 1982a). Additionally, a dermal study in rats reported an LD_{50} greater than 2000 mg/kg (Reported to the ECHA database, 1990c). These results provide sufficient information to indicate low concern for acute, dermal toxicity with LD_{50} values above the low-concern benchmark of 2000 mg/kg for dermal exposures.

A study on rats exposed via inhalation to 5.7 mg/L (734 ppm) of DPMA vapor for four hours and then observed for two weeks reported no mortalities (OECD, 2003; Reported to the ECHA database, 1982b). 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 mammalian toxicity from repeated exposures to DPMA using experimental data and read-across from analogs.

A study on rats exposed to DPMA by oral gavage for 28 days resulted in a no observed adverse effect level (NOAEL) of 1000 mg/kg-day (Reported to the ECHA database, 1990f). These results provide sufficient information to indicate low concern for repeated oral toxicity by exceeding the low-concern benchmark of 100 mg/kg-day for 90-day studies or 300 mg/kg-day for approximately 30-day studies.

Two studies on rabbits dermally exposed to dipropylene glycol, methyl ether for 90-days reported an NOAEL of 4750 mg/kg-day (Dow Chemical, 2000a) and a lowest observed adverse effect level (LOAEL) of 9500 mg/kg-day (Dow Chemical, 2000b; Rowe et al., 1954). Further, a study on rats dermally 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, because the body weight changes only occurred in males and the increased white blood cell count was due to inflammation, 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 DPMA has low concern for dermal repeated dose toxicity.

A 13-week inhalation study in rats and rabbits exposed to dipropylene glycol, methyl ether vapor reported no adverse effects at the highest tested concentration (1.212 mg/L), resulting in a no observed adverse effect concentration (NOAEC) of 1.212 mg/L (Landry and Yano, 1984). These

results provide 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 analogs to evaluate DPMA's potential to induce mammalian reproductive and developmental toxicity.

A one-generation reproductive study in rats exposed to dipropylene glycol monoethyl 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 also no 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 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 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) (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 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 DPMA's potential for gene mutation and chromosomal aberration as potential indicators of genotoxic carcinogenicity.

Two *in vitro* gene mutation studies in *Salmonella typhimurium* and *E. coli* exposed to DPMA resulted in negative findings with and without metabolic activation (OECD, 2003).

EPA used read-across from analogs to assess genotoxicity through other mechanisms. Tripropylene glycol monomethyl ether did not elicit unscheduled DNA synthesis in rat hepatocyte cells (Dow Chemical, 1982). A study on mice injected with dipropylene glycol monobutyl ether demonstrated negative results 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[32] on DPMA 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 DPMA. Structural alerts represent molecular functional groups or substructures that are known to be linked to the carcinogenic activity of chemicals. The most common structural alerts are those for electrophiles (either direct acting or following activation). Modulating factors that will impact the carcinogenic potential of a given electrophile will include its relative hardness or softness, its molecular flexibility or rigidity, and the balance between its reactivity and stability.[33]

For this chemical, there is an absence of the types of reactive structural features that are present in genotoxic carcinogens. DPMA is not an electrophile. ISS profiler, a QSAR model,[34] identified an alert for in vivo mutagenicity (micronucleus) via H-acceptor-path3-H-acceptor. The H-acceptor-path3-H-acceptor alert explores the possibility that a substance interacts with DNA/proteins by a non-covalent binding route such as DNA intercalation or groove binding. The percentage of true positives for this alert was low. For example, 34% of the substances that generate this alert tested positive for this mutagenic pathway (i.e., 55 substances tested positive of the 163 substances with this alert in the original analysis conducted by Benigni et al., 2009,[35]). Thus, the presence of this alert is not necessarily a strong indicator of effects. In addition, results from an *in vivo* mouse micronucleus study were negative for chromosomal aberrations in the analog dipropylene glycol monobutyl ether (OECD, 2003), providing sufficient information to suggest this chemical is unlikely to cause mutagenicity through the alert identified by the ISS Profile. Further, one of the Virtual models for property Evaluation of chemicals within a Global Architecture (VEGA) models'[36] results indicate dipropylene glycol butyl ether has low potential to be carcinogenic or mutagenic with moderate reliability.

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

[33] "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.

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

[35] Benigni, R. (2008). The Benigni/Bossa rule base for mutagenicity and carcinogenicity – A module of Toxtree. EUR 23241, 1-70.

[36] 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.

DPMA will undergo biotransformation through multiple metabolic pathways and subsequentially be excreted, making this alert of low concern (see Figure 4 (metabolic tree) in Metabolic Pathway Trees Supplemental Document[37]).

Applying expert scientific judgement based on the reasonably available information and weight of the scientific evidence, EPA finds that DPMA's transformation profile, low potential to be carcinogenic or mutagenic predictions, and negative 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 DPMA or closely-related analogs were available to assess the potential for DPMA to cause neurotoxicity. However, EPA assessed the potential for neurotoxicity using relevant endpoints measured in repeated dose studies and accepted NAMs, such as ToxCast.[38]

A repeated-dose study on rats exposed to dipropylene glycol monoethyl ether by oral gavage reported minimal effects on the limited neurological endpoints that were evaluated. Effects to hindlimb grip strength (magnitude of effect not reported) were observed in female rats at oral doses of dipropylene glycol monoethyl ether at 1000 mg/kg-day 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).

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

ToxCast assays related to neurological functions were not identified for DPMA. Results for tripropylene glycol n-butyl ether included 8 *in vitro* high-throughput biochemical- and cell-based assays related to neurological functions.[39] Bioactivity was not induced in any assay by tripropylene glycol n-butyl ether.

DPMA's low-concern findings for other human health hazard endpoints, including toxicity from acute and repeated exposures, and predictions by ToxCast, provide sufficient information to indicate low concern for neurotoxicity.

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

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

[39] 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.

6.1.8 Skin Sensitization

Experimental data determined to be of adequate quality[40] on DPMA 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 DPMA 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[41] on DPMA or closely-related analogs were not reasonably available for the assessment of respiratory sensitization potential. To model respiratory sensitization of DPMA, EPA used NAMs, such as the QSAR Toolbox, version 4.2 models[42] for keratinocyte gene expression; protein binding potency h-CLAT; protein binding potency cysteine; protein binding potency lysine; and respiratory sensitization. DPMA had one structural alert for non-conjugated carboxylic acids and esters, which was considered slightly positive based on a grey zone (9-21%) alert for protein binding potency of cysteine (Direct Peptide Reactivity Assay, 13%). While skin sensitizers bind to both lysine and cysteine residues, respiratory sensitizers are more likely to selectively react with lysine.[43] These results do not indicate any structural alerts for protein binding potency for lysine. The weight of the scientific evidence provides sufficient information to indicate low concern for respiratory sensitization potential for DPMA.

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 DPMA 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 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

[40] 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.

[41] 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.

[42] 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

[43] ECHA's Guidance on Information Requirements and Chemical Safety Assessment: https://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf/e4a2a18f-a2bd-4a04-ac6d-0ea425b2567f

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 DPMA.

6.1.11 Skin Irritation

EPA assessed dermal irritation effects using experimental data in rabbits. One study demonstrated DPMA induced slight erythema in one of six animals at 24 hours, but these effects were fully reversible by 72 hours (OECD, 2003; Reported to the ECHA database, 1982e). Another study reported DPMA as negative for inducing skin irritation (Reported to the ECHA database, 1990g). These studies provide sufficient information to indicate low concern for skin irritation.

6.1.12 Eye Irritation

To assess potential for eye irritation, EPA used the results of two studies on rabbits. Rabbits exposed to DPMA displayed erythema in three of six rabbits at 1 hour, but the effects were fully reversible by 24 hours (OECD, 2003; Reported to the ECHA database, 1982d). Another study reported negative results and indicated DPMA was non-irritating (Reported to the ECHA database, 1990e). These studies provide sufficient information to indicate low concern for eye irritation.

6.1.13 Hazards to Potentially Exposed or Susceptible Subpopulations

The above information supports a low human health hazard finding for DPMA 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 DPMA.

6.2 Environmental Hazard

To review environmental hazard endpoints without adequate quality[29] 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 DPMA based on available acute toxicity experimental data and estimated chronic toxicity values using the Ecological Structure Active (ECOSAR) Predictive Model.[44] 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 DPMA. Aquatic vertebrates exposed to DPMA resulted in an LC_{50} of 151 mg/L (OECD, 2003). Invertebrates exposed to DPMA resulted in an LC_{50} of 1090 mg/L (OECD, 2003; Reported to the ECHA database, 1983b). Algae exposed to DPMA resulted in an EC_{50} greater than 1000 mg/L (Reported to the ECHA database, 2000d). These results provide sufficient information to indicate low concern for acute aquatic exposure by exceeding the low-concern benchmark of 100 mg/L.

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

6.2.2 Chronic Aquatic Toxicity

Chronic toxicity values estimated using ECOSAR for aquatic vertebrates, invertebrates, and algae were 15 mg/L, 370 mg/L, and 32 mg/L respectively. These predicted toxicity values provide sufficient information to indicate that DPMA 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 DPMA using available experimental data on both ready biodegradation and inherent biodegradation.

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

In one stringent ready test similar to OECD 301C, using a test concentration of 100 mg/L, DPMA did not pass the criteria based on O_2 consumption and was considered not readily biodegradable under aerobic conditions (OECD, 2003; Reported to the ECHA database, 2000c). However, 100% primary degradation was observed in this test, indicating that the parent compound is not persistent under the conditions of this test. In addition, results from modified ready biodegradation tests using adapted and acclimated inocula verify that DPMA is ultimately biodegradable under aerobic conditions (OECD, 2003; Reported to the ECHA database, 1996). In addition, tripropylene glycol n-butyl ether, a closely related analog, passed two OECD 301-series ready tests under aerobic conditions and was considered readily biodegradable. Tripropylene glycol n-butyl ether met the 10-day window at a concentration of 90 mg/L in the OECD 301F test, but did not meet the 10-day window at 32 mg/L in the OECD 301F test (Dow Chemical, 1998; Reported to the ECHA database, 1998a) and 20 mg DOC/L in the OECD 301A test (Reported to the ECHA database, 2002). Based on structural analysis, tripropylene glycol n-butyl ether is expected to degrade at a slower rate compared to DPMA because it has more propylene glycol ether groups. Based on this analysis, DPMA can be considered readily biodegradable by analogy to tripropylene glycol n-butyl ether. An inherent biodegradability test OECD 302B (Reported to the ECHA database, 1993) for tripropylene glycol n-butyl ether and a BOD5 test for DPMA (Reported to the ECHA database, 1983a) provide additional evidence that these substances are at least inherently and ultimately biodegradable under aerobic conditions. Furthermore, the microbial inhibition tests indicate that these substances are non-toxic to microbial populations found in sewage treatment plants (Reported to the ECHA database, 2000e).

Anaerobic biodegradation data were not available for DPMA; however, an anaerobic study was available for a closely-related analog. In an OECD 311 equivalent test, the analog 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 ISO11734 anaerobic test,[45] 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)[46]. For DPMA, the chemical substance contains degradable functional groups such as aliphatic ethers and carboxylic acids/esters. The aliphatic ether functional group could anaerobically break down via O-demethylation by O-demethylase enzymes (Ghattas et al., 2017)[46]. Rorije et al. (2009)[47] also identified a methoxy-substituent as a potential biophore that is amenable to anaerobic biodegradation. Anaerobic biodegradation of carboxylic acids can occur via beta-oxidation, similar to the aerobic pathway since oxygen is not directly involved, if the carboxylic acid is at the terminus of the aliphatic chain and not sterically hindered at the alpha or beta carbon (Ghattas et al, 2017[46]). While EPA cannot be certain of the rates at which these anaerobic pathways may occur, this information supports the potential for DPMA to anaerobically biodegrade based on DPMA's structure. In addition, DPMA's low-hazard results for environmental and mammalian toxicity and evidence of aerobic biodegradation indicate low concern for this chemical if present in anaerobic environments.

No degradation products of concern were identified for this chemical substance. Applying expert scientific judgement based on the reasonably available information and weight of the 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 1.1 using the Estimation Programs Interface (EPI) Suite models,[48] EPA has sufficient information that DPMA has low potential for bioaccumulation in the environment based on the low-concern benchmark of less than 1000.

[45] 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)

[46] 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

[47] Rorije, E., Peijnenburg, W.J. and Klopman, G. (1998), Structural requirements for anaerobic biodegradation of organic chemicals: A fragment model analysis. *Environmental Toxicology and Chemistry*, 17: 1943-1950. doi:10.1002/etc.5620171008. Available at: https://setac.onlinelibrary.wiley.com/action/showCitFormats?doi=10.1002%2Fetc.5620171008

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

7. Exposure Characterization

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

As shown in Tables 3 and A.3, DPMA is a solvent used in processing (incorporation into an article and into a formulation, mixture, or product) in the paints, coatings, and industrial printing ink manufacturing sectors. 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 DPMA is based on an analysis of the CDR from 1986 to 2015.[49] Prior to 2011, DPMA was not reported in the CDR. This does not mean it was not being produced or imported, but more likely that no single entity site was producing above the reporting threshold of generally 25,000 lb. per site per year. Between reporting years 2011 and 2013, aggregate production volume for DPMA was between 1,000,000 and 10,000,000 lbs., and in reporting years 2014 and 2015 between 10,000,000 and 50,000,000 lbs. of DPMA was produced or imported.

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 DPMA. Exposure is also possible from other activities, such as distribution and disposal. These activities could result in releases of DPMA to media including surface water, landfills, and air.

EPA expects high levels of removal of DPMA 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, DPMA is expected to have low persistence (aerobic biodegradation is discussed in Section 6.3.1) and has the potential to break down in the environment into carbon dioxide and water. Therefore, any release of this chemical 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), DPMA is expected to have negligible adsorption to sediment, reducing the potential toxicity to benthic organisms.

[49] 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.

DPMA'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 DPMA to the point that it will not be present in air.

7.3 Exposures to the General Population

EPA expects the general population is unlikely to be exposed to DPMA from the potential environmental releases described above. Air exposure is unlikely from incineration. If DPMA is present in the air from volatilization, it is expected to be reduced because of its short atmospheric half-life of less than 4 hours (see Table 2 in Section 3). DPMA is unlikely to be present in surface water because it will degrade (discussed in Section 6.3.1), reducing the potential for the general population to be exposed by oral ingestion or dermal exposure. Further, given the low bioaccumulation or bioconcentration potential of DPMA, oral exposure to DPMA 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 DPMA than the general population during manufacturing, processing, distribution, use, and disposal. EPA identified consumers as a population that may experience greater exposure to DPMA than the general population through use of ink, toner, and colorant products; laundry and dishwashing 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), DPMA is a liquid under ambient conditions. Based on DPMA'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, DPMA is expected to be volatile at ambient temperatures, and therefore workers may be exposed through inhalation of vapors. However, if DPMA is in a dilute form, the estimated Henry's Law constant for DPMA suggests volatilization from water and aqueous solutions is expected to be minimal. Workers may be exposed to DPMA in manufacturing, processing, distribution, use, and disposal.

7.4.2 Exposures to Consumers

Consumers may be exposed to DPMA through the use of ink, toner, and colorant products, laundry and dishwashing products; cleaning and furnishing care products; adhesives and sealants; and anti-freeze and de-icing products, among others (Table 3). For all these uses, if dermal contact does occur, DPMA is expected to have poor to moderate absorption through the skin based on its molecular weight, water solubility and partitioning coefficient (Section 3) and experimental data (Section 6.1.1). If the chemical is in an aerosol product and inhalation exposure occurs, DPMA's absorption from the lungs is likely. EPA does not include intentional misuse, such as people drinking products containing this chemical, as part of the known, intended or reasonably foreseen conditions of use that could lead

to an exposure (82 FR 33726). Thus, oral exposures will be incidental (meaning inadvertent and low in volume). DPMA 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 DPMA 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 DPMA. EPA used this information to inform its determination of whether DPMA meets the statutory criteria and considerations for final designation as a low-priority substance.

- **Hazard potential:**

For DPMA'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 DPMA is of low concern for human health and environmental hazard across a 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, consumers, and workers may be exposed to DPMA, exposure by the dermal pathway is limited by DPMA's physical-chemical properties. If ingestion occurs, DPMA is expected to be metabolized and excreted, reducing the duration of exposure. Inhalation of DPMA in dilute products is expected to be minimal; however, workers may be exposed to vapors of neat DPMA. If DPMA is released into the environment, its exposure potential will be reduced through biodegradation.

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

Conclusion: Based on an initial analysis of reasonably available hazard and exposure information, EPA concludes that the risk-based screening-level review under 40 CFR 702.9(a)(1) does not support a finding that DPMA 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 DPMA 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 DPMA is readily and inherently biodegradable under aerobic conditions (discussed in Section 6.3.1). 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 DPMA 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 DPMA 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, laundry and dishwashing 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 DPMA than the general population. Because of the chemical's low-concern hazard properties, 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 DPMA 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 DPMA 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 DPMA 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, DPMA 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, DPMA 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 DPMA 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, DPMA would degrade in aerobic environments (see Section 6.3.1). 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 DPMA 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 DPMA under 40 CFR 702.9(a)(4) does not support a finding that DPMA 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 DPMA and related potential exposures and hazards.

Rationale: EPA evaluated the conditions of use of DPMA (see Section 5 and Appendix A) and found it to have a broad range of conditions of use.

EPA expects that even if the conditions of use were to expand beyond activities that are currently known, intended and reasonably foreseen, the outcome of the screening review would likely not change and would not alter the Agency's conclusion of low concern. EPA bases this expectation on DPMA'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 DPMA 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 DPMA 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 DPMA (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 DPMA as a low-priority substance could result in increased use and higher production volumes. EPA expects, however, that any changes in DPMA'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 DPMA'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, DPMA does not meet the standard for a high-priority substance. The reasonably available information on production volume, or significant changes in production volume, described above provides sufficient information to support this finding.

8.7. Other Considerations

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

9. Final Designation

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

Appendix A: Conditions of Use Characterization

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

A.1. CDR Manufacturers and Production Volume

The Chemical Data Reporting (CDR) rule (previously known as the Inventory Update Rule, or IUR), under TSCA section 8, requires manufacturers (including importers) to report information on the chemical substances they produce domestically or import into the U.S., generally above a reporting threshold of 25,000 lb. per site per year. According to the 2016 Chemical Data Reporting (CDR) database, 31 companies manufactured or imported DPMA at 31 sites for reporting year 2015.

Table A.1 presents the historic production volume of DPMA from the CDR (previously known as the Inventory Update Rule, or IUR) from 1986-2015. Prior to 2011, DPMA was not reported in the CDR. This does not mean it was not being produced or imported, but more likely that no single entity site was producing above the reporting threshold. Between reporting years 2011 and 2013, aggregate production volume for DPMA was between 1,000,000 and 10,000,000 lbs., and in reporting years 2014 and 2015 between 10,000,000 and 50,000,000 lbs. of DPMA was produced or imported.

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

1986	1990	1994	1998	2002	2006	2011	2012	2013	2014	2015
Unknown[1]						1 M – 10 M	1 M – 10 M	1 M – 10 M	10 M – 50 M	10 M – 50 M

Source(s):
EPA (2018a; 2017b; 2006; 2002)
Note(s):
K = Thousand; M = Million; NDR = No data reported
1. The CAS RN 88917-22-0 could not be found in the 2006 or 1986-2002 IUR. It is possible that no single entity triggered the reporting threshold in this year.

A.2. Uses

A.2.1 Methods for Uses Table

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

Table A.2: Sources Searched for Uses of DPMA

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)	88917-22-0	No
Canada Chemicals Management Plan information sheets	Government of Canada (2018)	88917-22-0	No
Chemical and Product Categories (CPCat)	CPCat et al. (2015)	88917-22-0	Yes
ChemView [2]	EPA (2018a)	88917-22-0	Yes
Children's Safe Product Act Reported Data	Washington State Dept. of Ecology (2018)	88917-22-0	No
Consumer Product Information Database (CPID)	DeLima Associates (2018)	88917-22-0	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)	Dipropylene glycol methyl ether acetate	Yes
DrugBank	DrugBank (2018)	Dipropylene glycol methyl ether acetate; 88917-22-0	No
European Chemicals Agency (ECHA) Registration Dossier	ECHA (2018)	88917-22-0	Yes
eChemPortal [2]	OECD (2018)	88917-22-0	No
Envirofacts [2]	EPA (2018b)	88917-22-0	No
Functional Use Database (FUse)	EPA (2017a)	88917-22-0	Yes
Kirk-Othmer Encyclopedia of Chemical Technology	Kirk-Othmer (2006)	Dipropylene glycol methyl ether acetate; 88917-22-0	No
Non-Confidential 2016 Chemical Data Reporting (CDR)	EPA (2017b)	88917-22-0	Yes

Table A.2: Sources Searched for Uses of DPMA			
Title	**Author and Year**	**Search Term(s)**	**Found Use Information?[1]**
PubChem Compound	Kim et al. (2016)	88917-22-0	Yes
Safer Chemical Ingredients List (SCIL)	EPA (2018d)	88917-22-0	Yes
Synapse Information Resources [2]	Synapse Information Resources (2009)	Dipropylene glycol methyl ether acetate	Yes
Resource Conservation and Recovery Act (RCRA)	EPA (2018c)	DPMA; dipropylene; glycol ether	No
Scorecard: The Pollution Information Site	GoodGuide (2011)	88917-22-0	No
Skin Deep Cosmetics Database	EWG (2018)	88917-22-0	No
Toxics Release Inventory (TRI)	EPA (2018e)	88917-22-0	No
TOXNET [2]	NLM (2018c)	88917-22-0	Yes
Ullmann's Encyclopedia of Industrial Chemistry	Ullmann's (2000)	Dipropylene glycol methyl ether acetate; 88917-22-0	No
Additional sources identified from reasonably available information			
Chemical Consultants Inc.	Chemical Consultants Inc. (2018)	Incidentally identified while researching into details of this chemical's uses and products.	Yes
Dow Chemical Company (Dow)	Dow (2015)		
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 398 patents referencing "dipropylene glycol methyl ether acetate" (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 DPMA 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 DPMA

Table A.3: Uses of DPMA		
Use	**Expected Users**	**Description of Use and References**
TSCA Conditions of Use: Automotive and Transportation		
Auto and tire care	Industrial	CPCat (2019) CPCat reports use of DPMA in retail automotive care and cleaning products, repair, fluids and lubricants, and tire accessories. Expected users are industrial.
Tire protectant	Consumer	NLM (2018b); Meguiars Inc. (2008) The Household Products Database identifies one tire protectant product that contains DPMA. The Household Products Database generally includes consumer products; therefore, the expected users are consumer.
Trade and repair of motor vehicles and motorcycles	Industrial	SPIN (2018) SPIN reports use of DPMA in the wholesale and retail trade and repair of motor vehicles and motorcycles in Nordic countries. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are industrial based on inclusion in SPIN's industrial uses database.
Transport activities	Industrial	SPIN (2018) SPIN reports use of DPMA in supporting and auxiliary transport activities (including warehousing), as well as activities of travel agencies, in Nordic countries. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are industrial based on inclusion in SPIN's industrial uses database.

Table A.3: Uses of DPMA		
Use	**Expected Users**	**Description of Use and References**
Transportation equipment manufacturing	Industrial	SPIN (2018) SPIN reports use of DPMA in the manufacture of other transport equipment in Nordic countries. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are industrial based on inclusion in SPIN's industrial uses database.
TSCA Conditions of Use: Cleaning CDR reports use of liquid DPMA in consumer and commercial cleaning and furnishing care products. CDR reports concentrations (by weight) of less than one percent in consumer products, at least 90 percent in commercial products, and at least one percent but less than 30 percent in consumer and commercial products (EPA 2017b). ECHA identifies use of DPMA in commercial washing and cleaning products in European countries (Reported to the ECHA database, 2018).		
Air care products	Consumer	EPA (2017b); DeLima Associates (2015); CPCat (2019); Reported to the ECHA database, 2018 CDR reports use of liquid DPMA in consumer air care products at concentrations (by weight) of less than 30 percent and at least 90 percent. CDR does not define what is included in air care products, however this category generally includes air fresheners, candles, etc. CPID lists multiple air fresheners that contain DPMA. ECHA identifies use of DPMA in air care products in European countries. Expected user is consumer based on CDR's consumer/commercial classification.
Laundry and dishwashing products	Consumer	EPA (2017b) CDR reports use of DPMA in consumer laundry and dishwashing products at concentrations of less than one percent by weight. Expected users are consumer based on CDR's consumer/commercial classification.

Table A.3: Uses of DPMA		
Use	**Expected Users**	**Description of Use and References**
Penetrating solvent/lubricant	Consumer, commercial	DeLima Associates (2014); CPCat (2019); Monument Chemical (2018); Synapse Information Resources (2009) Monument Chemical identifies DPMA as a solvent used for dissolving resins in paints, coatings, lacquers, and inks. Synapse Information Resources identifies use in cleaning solvents and as a soil penetrant in cleaners. CPID lists one commercial penetrating solvent that contains DPMA. Expected user is consumer and commercial based on CDR's consumer/commercial classification.
Soap, cleaning compound, and toilet preparation manufacturing	Industrial	EPA (2017b) CDR reports use of DPMA as a solvent and odor agent in processing during soap, cleaning compound, and toilet preparation manufacturing. Expected users are industrial based on inclusion in CDR's Industrial Processing and Use report.
TSCA Conditions of Use: Media		
Ink, toner, and colorant products	Consumer, commercial, industrial	EPA (2017b); Monument Chemical (2018); Synapse Information Resources (2009); NLM (2018a); Reported to the ECHA database, 2018; Dow (2015); SPIN (2018); Dow (2017) CDR reports use of liquid DPMA in ink, toner, and colorant products at concentrations of at least one percent but less than 30 percent by weight. CDR also reports use of liquid DPMA as a solvent in processing during printing ink manufacturing. Monument Chemical and Haz-Map identify use of DPMA in silk screen inks, while Dow and Synapse Information Resources identify use as a solvent for (silk screen) inks. ECHA identifies use of DPMA in consumer inks and toners as well as ink mixing, transferring in European countries. SPIN reports use of DPMA in printing inks, dyestuff, pigments, and coloring agents in Nordic countries. Expected consumers are consumer and commercial based on CDR's consumer/commercial classification and industrial based on CDR's Industrial Processing and Use report.

Table A.3: Uses of DPMA		
Use	**Expected Users**	**Description of Use and References**
Photo-chemicals and reprographic agents	Consumer, commercial, industrial	SPIN (2018) SPIN reports use of DPMA in photo-chemicals and reprographic agents in Nordic countries. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are assumed to be consumer, commercial, and industrial.
Printing and reproduction of recorded media	Industrial	SPIN (2018) SPIN identifies use of DPMA by publishers and printers and for printing and reproduction of recorded media in Nordic countries. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are industrial based on inclusion in SPIN's industrial uses database.
Screen printing and roll coating	Industrial	Reported to the ECHA database, 2018 The ECHA registration dossier identifies use of DPMA in screen printing and roll coating processes by industrial users in European countries. Expected users are industrial based on inclusion in ECHA's uses at industrial sites.
Screen wash	Consumer, commercial, industrial	Chemical Consultants Inc. (2018) Chemical Consultants Inc. identifies use of DPMA in screen wash to dissolve UV-, Plastisol-, and water-based inks. Expected users are assumed to be consumer, commercial, and industrial.
TSCA Conditions of Use: Other Manufacturing		
Chemical manufacturing	Industrial	SPIN (2018) SPIN reports use of DPMA in the manufacture of chemicals and chemical products in Nordic countries. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are industrial based on inclusion in SPIN's industrial uses database.

Table A.3: Uses of DPMA		
Use	**Expected Users**	**Description of Use and References**
Manufacture of rubber and plastic products	Industrial	SPIN (2018) SPIN reports use of DPMA in the manufacture of rubber and plastic products in Nordic countries. No further information about this use could be found, and it is unknown whether this is an ongoing use in the United States. Expected users are industrial based on inclusion in SPIN's industrial uses database.
TSCA Conditions of Use: Miscellaneous		
Adhesives	Consumer	Synapse Information Resources (2009); Reported to the ECHA database, 2018 Synapse Information Resources identifies use of DPMA as a coupling agent and as a solvent for adhesives. ECHA identifies use of DPMA in adhesives and sealants in European countries. Expected users are consumer based on inclusion in ECHA's consumer uses.
Anti-freeze and de-icing products	Consumer	Reported to the ECHA database, 2018 The ECHA registration dossier identifies use of DPMA in anti-freeze and de-icing products in European countries. Expected users are consumer based on inclusion in ECHA's consumer uses.
Electronics	Consumer, commercial, industrial	Synapse Information Resources (2009) Synapse Information Resources identifies use of DPMA as a solvent for electronic chemicals. Expected users are assumed to be consumer, commercial, and industrial.
Fragrance	Industrial	EPA (2017b); Reported to the ECHA database, 2018 CDR reports use of liquid DPMA as an odor agent in the processing of fragrances, and ECHA identifies use of DPMA in perfumes and fragrances in European countries. The International Fragrance Association does not list DPMA as a current ingredient in its list of standards. Expected users are industrial based on inclusion in CDR's Industrial Processing and Use report.

Table A.3: Uses of DPMA		
Use	**Expected Users**	**Description of Use and References**
Lubricants, greases, and release products	Consumer	Reported to the ECHA database, 2018 ECHA identifies use of DPMA in lubricants, greases, and release products in European countries. Expected user is consumer based on inclusion in ECHA's consumer uses.
Mining	Consumer, commercial, industrial	Synapse Information Resources (2009) Synapse Information Resources identifies use of DPMA as a solvent for mining uses. Expected users are assumed to be consumer, commercial, and industrial.
Oil field	Unknown	Synapse Information Resources (2009) Synapse Information Resources identifies use of DPMA as a solvent for oil field uses. No further information on this use could be found. Expected users are unknown, due to the limited availability of information.
Paints and coatings	Consumer, commercial, industrial	EPA (2017b); Monument Chemical (2018); Synapse Information Resources (2009); NLM (2018a); Reported to the ECHA database, 2018; Dow (2015); SPIN (2018) CDR reports use of liquid DPMA in paints and coatings at concentrations of at least 90 percent by weight in commercial products and at least one percent but less than 30 percent by weight in consumer and commercial products. CDR also reports use of DPMA as a solvent in paint and coating manufacturing. Monument Chemical identifies use of DPMA as a solvent in paints and coatings. Synapse Information Resources identifies use as a solvent for paints and epoxy laminates and as a coalescent for architectural water-borne coatings. Haz-Map identifies use of DPMA as an active and tailing solvent in coatings. ECHA identifies use of DPMA in coatings and paints, thinners, and paint removers in European countries, and SPIN reports use in paints, lacquers, and varnishes in Nordic countries. Dow identifies use of DPMA as an industrial solvent for automotive paints and coatings (topcoats and refinishing), coil coatings (protective finish), industrial maintenance coatings (corrosion control) and metal finishes. Expected consumers are consumer and commercial based on CDR's consumer/commercial classification and industrial based on CDR's Industrial Processing and Use report.

Table A.3: Uses of DPMA		
Use	**Expected Users**	**Description of Use and References**
Polishes	Consumer	Synapse Information Resources (2009); Reported to the ECHA database, 2018 Synapse Information Resources identifies use of DPMA as a solvent for floor polishes. ECHA identifies use of DPMA in polishes and wax blends in European countries. Expected user is consumer based on inclusion in ECHA's consumer uses.
Surface treatment	Consumer	Synapse Information Resources (2009); Reported to the ECHA database, 2018 Synapse Information Resources identifies use of DPMA as a wetting agent. ECHA identifies use of DPMA in non-metal surface treatment products in European countries. Expected user is consumer based on inclusion in ECHA's consumer uses.
Textiles	Consumer	Reported to the ECHA database, 2018 ECHA identifies use of DPMA in leather treatment products, textile dyes, and impregnation products in European countries. Expected user is consumer based on inclusion in ECHA's consumer uses.
Welding, soldering, and flux products	Consumer	Reported to the ECHA database, 2018 ECHA identifies use of DPMA in welding, soldering, and flux products in European countries. Expected user is consumer based on inclusion in ECHA's consumer uses.
Wholesale and retail trade	Industrial	EPA (2017b) CDR reports use of liquid DPMA as a solvent in repackaging during wholesale and retail trade. Expected users are industrial based on inclusion in CDR's Industrial Processing and Use report.

Table A.3: Uses of DPMA		
Use		**Description of Use and References**
Non-TSCA Uses		
Agriculture	Consumer	Synapse Information Resources (2009); Reported to the ECHA database, 2018 Synapse Information Resources identifies use of DPMA as a solvent for agricultural uses. ECHA identifies use of DPMA in biocidal products in European countries. Expected users are consumer based on inclusion in ECHA's consumer uses.
Personal care products	Consumer, commercial	EPA (2017b); DeLima Associates (2016) CDR reports use of liquid DPMA in commercial personal care products at concentrations of at least 90% by weight. CPID identifies one consumer hair product that contains DPMA. Expected users are commercial based on CDR's consumer/commercial classification, and consumer based on CPID.
Children's Products		
CDR reports did not include any uses in children's products; however, use in children's hair conditioner is found in this table.		
Recycling and Disposal		
In the 2016 CDR, one facility (CBI) reported that DPMA was recycled (recycled, remanufactured, reprocessed, or reused). Nineteen facilities reported that DPMA was not recycled, while eight facilities withheld this information and three reported it as CBI.		

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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**
5016019	Oral (gavage)	Sprague Dawley rats	Single exposure,14 day observation	**Dose:** 5000 mg/kg **Replicates:** 5 per sex	**LD_{50}** > 5000 mg/kg	**Methods:** • Test substance reported as CASRN 88917-22-0 • Purity not reported • OECD Guideline 401 • GLP compliant
5015995, 4956637, 2530089	Oral (gavage)	Fischer F344 rats	Single exposure, 14 day observation	**Doses:** Male and female: 630, 1300, 2500, 5000 and Female: 10000 mg/kg **Replicates:** 6 per sex per group	**Female: LD_{50}**: 5448 mg/kg (95% CI 4071-7635) **Male: LD_{50}** > 5000 mg/kg	**Methods:** • Test substance reported as CASRN 88917-22-0 • Purity not reported • Equivalent to OECD Guideline 401 • GLP compliant **Mortalities:** • 5000 mg/kg: 2/6 females • 100000 mg/kg: 6/6 females
4956637, 5016017	Dermal	New Zealand White rabbits	24 hour exposure, 14 day observation	**Dose:** 5000 mg/kg **Replicates:** 2 per sex	**LD_{50}** > 5000 mg/kg	**Methods:** • Test substance reported as CASRN 88917-22-0 • Purity not reported • Equivalent to OECD Guideline 402 • GLP compliant
5016008	Dermal	Sprague-Dawley rats	24 hour exposure, 14 day observation	**Doses**: 500, 100, 1500, and 2000 mg/kg **Replicates:** 2 per sex per group, additional 5 Rats exposed to 2000 mg/kg	**LD_{50}** > 2000 mg/kg	**Methods** • Test substance reported as CASRN 88917-22-0 • Purity not reported • OECD Guideline 402 • GLP compliance not reported

Table B.1: Human Health Hazard						
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
Repeated Dose Toxicity						
Source	**Exposure Route**	**Species & strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
5016010	Oral (gavage)	Sprague Dawley rats	28 days	**Doses:** 0, 100, 250 and 1000 mg/kg-day **Replicates:** 5 per sex per dose	**NOAEL:** 1000 mg/kg-day	**Methods:** • Test substance reported as CASRN 88917-22-0 • Purity not reported • Equivalent to OECD Guideline 407 • GLP compliant
4946620	Inhalation	Fisher 344 rats	13 weeks	**Doses:** 0, 0.091, 0.393, and 1.212 mg/L-day **Replicates:** 10 per group per sex	**NOAEC:** 1.212 mg/L-day	**Methods:** • Test substance reported as CASRN 34590-94-8 • Purity: 99% • GLP compliance not reported
4946620	Inhalation	New Zealand White rabbits	13 weeks	**Doses:** 0, 0.091, 0.393, and 1.212 mg/L-day **Replicates:** 7 per group per sex	**NOAEC:** 1.212 mg/L-day	**Methods:** • Test substance reported as CASRN 34590-94-8 • Purity: 99% • 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

Table B.1: Human Health Hazard						
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
3041622, 4944882	Dermal	Rabbits	90 days	**Doses:** 0, 1, 3, 5, and 10 mL/kg-day **Replicates:** 5 males per group	**NOAEL**: 5 mL/kg-day, **LOAEL**: 10 mL/kg-day; equivalent to 9500 mg/kg-day based on mortality	**Methods:** • Test substance reported as CASRN 34590-94-8 • Purity not reported • GLP compliance not reported
4944882, 5077872, 4956637	Dermal	Rabbits	90 days	**Doses:** 0, 960, 2900, 4800, 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 • Pre-dates GLP compliance
4956637	Dermal	Wistar rats	13 weeks, 5 days per week	**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 increases in white blood cell counts in both sexes	**Methods:** • Test substance reported as CASRN 29911-28-2 • Purity > 95% • GLP compliance not reported

Table B.1: Human Health Hazard						
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 **Results:** • Not maternally toxic, embryo- or fetotoxic, or teratogenic in Wistar rats receiving dermal doses up to highest dose.
5077932	Inhalation	Albino rat	GD 6-15	**Doses:** 0, 0.3, 0.9, 2.7, and 8.9 mg/L-day **Replicates:**	**NOAEC:** 8.9 mg/L-day	**Methods:** • Test substance reported as CASRN 25498-49-1

Table B.1: Human Health Hazard						
				7 females per dose		• Purity: 98.5% • GLP compliance not reported
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
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 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.

Table B.1: Human Health Hazard		
ISS v2.4[50]	Negative (Estimated) DPMA 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:** • Alert for an H-acceptor-path3-H-acceptor for in vivo mutagenicity (micronucleus) (see Figure 4 metabolic tree in Metabolic Pathway Trees Supplemental Document[51]).
VEGA 1.1.4[52]	DMPA was processed through all 4 models. IRFMN/Antares 1.0.0 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 (DPMA could lie outside of the AD) • ISS 1.0.2: Low reliability (DPMA could lie outside of the AD) • IRFMN/Antares 1.0.0: Moderate reliability (DPMA could lie outside of the AD) • IRFMN/ISSCAN-GX 1.0.0: Low reliability (DPMA could lie outside of the AD)

[50] 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).

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

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

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

Table B.1: Human Health Hazard						
Genotoxicity						
Source	**Test Type & endpoint**	**Species & strain (if available)**	**Metabolic activation**	**Doses and controls**	**Results**	**Study Details**
4956637	Gene mutation (*in vitro*)	Salmonella typhimurium strains TA98, TA100, TA1535, and TA1537	With and without	**Doses:** 0, 313, 635, 1250, 2500, and 5000 µg/plate	Negative	**Methods:** • Test substance reported as CASRN 88917-22-0 • Purity > 99% • KIHATSU Guidance 603 • GLP compliant
4956637	Gene mutation (*in vitro*)	E. coli strain WP2uvrA	With and without	**Doses:** 0, 313, 635, 1250, 2500, and 5000 µg/plate	Negative	**Methods:** • Test substance reported as CASRN 88917-22-0 • Purity > 99% • KIHATSU Guidance 603 • 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

Table B.1: Human Health Hazard						
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 • 0, 1000, 2000, 3000, and 4000 µg/mL without activation	Positive at cytotoxic concentrations (3332 µg/mL with activation)	**Methods:** • Test substance reported as CASRN 29911-28-2 • Purity > 95% • GLP compliant **Results:** • Cytotoxicity observed at 1000 and 3332 µg/mL with metabolic activation and 3000 and 4000 µg/mL without metabolic activation

Table B.1: Human Health Hazard						
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 • The 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

Table B.1: Human Health Hazard						
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), 225 mg/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 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.

Table B.1: Human Health Hazard						
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**
4956637, 5016018	Dermal	New Zealand White rabbits	Exposure for 24 hours, observed for 72 hours	**Dose:** 0.5 mL undiluted test substance **Replicates:** 6 females	Negative	**Methods:** • Test substance reported as CASRN 88917-22-0 • Purity not reported • OECD Guideline 404 • GLP compliant **Results:** • At 24 hours: 1/6 animals showed slight erythema • Effects fully reversible after 72 hours
5016007	Dermal	New Zealand White rabbits	Exposure for 4 hours, observed for 72 hours	**Dose:** 0.5 mL undiluted test substance **Replicates:** 3 total (2 males, 1 female)	Negative	**Methods:** • Test substance reported as CASRN 88917-22-0 • Purity not reported • OECD Guideline 404 • GLP not reported

Table B.1: Human Health Hazard						
4956637, 5016014	Ocular	New Zealand White rabbits	7 day observation	**Dose:** 0.1 mL **Replicates:** Unwashed: 6 Females Washed: 2 females & 1 male	Negative	**Methods:** • Test substance reported as CASRN 88917-22-0 • Purity not reported • OECD Guideline 405 • Not GLP compliant **Results:** • At 1 hour: 3/6 animals had erythema in unwashed group • Effects fully reversible after 24 hours
5016013	Ocular	New Zealand White rabbits	72 hour observation	**Dose:** 0.1 mL **Replicates:** 3 total (2 males, 1 female)	Negative	**Methods:** • Test substance reported as CASRN 88917-22-0 • Purity not reported • OECD Guideline 405 • GLP compliant
Immunotoxicity						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
5016010	Oral (gavage)	Sprague Dawley rats	28 days	**Doses:** 0, 100, 250 and 1000 mg/kg-day **Replicates:** 5 per sex per dose	**NOAEL:** 1000 mg/kg-day	**Methods:** • Test substance reported as CASRN 88917-22-0 • Purity not reported • Equivalent to OECD Guideline 407 • GLP compliant **Results:** • No treatment-related change in hematology and lymphoid tissue.

Table B.1: Human Health Hazard						
4946620	Inhalation	Fisher 344 rats	13 weeks	**Doses:** 0, 0.091, 0.393, and 1.212 mg/L-day **Replicates:** 10 per group per sex	**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 group per sex	**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.
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.

Table B.1: Human Health Hazard						
3041622, 4944882	Dermal	Rabbits	90 days	**Doses:** 0, 1, 3, 5, and 10 mL/kg-day **Replicates:** 5 males per group	**NOAEL**: 9500 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, gross pathology and organ weight related to lymphoid tissue.
4944882, 5077872, 4956637	Dermal	Rabbits	90 days	**Doses:** 0, 960, 2900, 4800, 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 • Pre-dates GLP compliance **Results:** • No treatment related changes in hematology and lymphoid tissue.
4956637	Dermal	Wistar rats	13 weeks, 5 days per week	**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 increases in white blood cell counts in both sexes	**Methods:** • Test substance reported as CASRN 29911-94-8 • Purity > 95% • GLP compliance not reported **Results:** • Increased white blood cell (neutrophil) counts in the 273 and 910 mg/kg-day treatment group.

Table B.2: Environmental Hazard					
Aquatic Toxicity: Experimental					
Source	**Species & strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
4956637, 4985129	*Pimephales promelas*	96 hours	**Doses:** 0, 100, 125, 160, 200, 250 and 320 mg/L (nominal)	**LC_{50}**: 151 mg/L nominal (calculated) (95% CI 139 - 161 mg/L)	**Methods:** • Test substance CASRN 88917-22-0 • Purity: 99.4% • OECD Guideline 203 • GLP compliant
4956637, 4985124	*Daphnia magna*	48 hours	**Doses:** 0, 160, 250, 400, 630, 1000, 1600, and 2500 mg/L (nominal)	**LC_{50}**: 1090 mg/L (nominal)	**Methods:** • Test substance CASRN 88917-22-0 • Purity: 99.4% • OECD Guideline 202 • GLP compliant
4985118	*Pseudokirchneriella subcapitata*	72 hours	**Doses:** 0, 1, 10, 100 and 1000 ppm (nominal)	**EC_{50}** > 1000 mg/L (nominal)	**Methods** • Test substance reported as CASRN 88917-22-0 • Purity not reported • OECD Guideline 201 • GLP compliance not reported
Aquatic Toxicity: Estimated					
Model	**Endpoint**	**Species**	**Predicted Effect Level**	**Notes**	
ECOSAR v2.0 (Class: Esters)	Chronic value	Freshwater fish	15 mg/L	SMILES Input: O=C(C)OC(C)COC(C)COC. Experimental input value: WS = 1.94E+5 mg/L.	
ECOSAR v2.0 (Class: Esters)	Chronic value	Daphnia magna	370 mg/L	SMILES Input: O=C(C)OC(C)COC(C)COC. Experimental input value: WS = 1.94E+5 mg/L.	
ECOSAR v2.0 (Class: Esters)	Chronic value	Green algae	32 mg/L	SMILES Input: O=C(C)OC(C)COC(C)COC. Experimental input value: WS = 1.94E+5 mg/L.	

Table B.3: Fate					
Environmental Fate: Experimental					
Source	**Endpoint**	**Duration**	**Doses and number of replicates**	**Results**	**Study Details**
4985139, 4956637	Biodegradation	28 days	**Dose:** 100 mg/L	Not readily biodegradable	**Methods:** • Test substance reported as CASRN 88917-22-0 • Purity: 99% • Japanese Guidelines "Biodegradation test of chemical substance by microorganisms etc." • GLP compliant **Results:** • Degradation: 16% biodegradation by O2 consumption after 28 days using an activated sludge inoculum • Nearly 100% conversion of DPMA to DPM without further degradation
4956637, 4985142	Biodegradation	28 days	**Doses:** 3.75 and 7.5 mg/L	Readily biodegradable	**Methods:** • Test substance reported as CASRN 88917-22-0 • Purity not reported • Similar to OECD 301D but used pre-adapted sludge • GLP compliant **Biodegradation results:** • 3.75 mg/L: 84.4% and 94.0% O2 consumption after 28 and 43 days, respectively • 7.5 mg/L: 58% and 73.3% O2 consumption after 28 and 43 days
4985133	Biodegradation	28 days	**Doses:** 3.75 and 7.5 mg/L	Readily biodegradable	**Methods:** • Test substance reported as CASRN 88917-22-0 • Purity: 99.4% • BOD 5 • GLP compliant **Biodegradation results:** • Activated industrial sludge inoculum: 67% after 28 days • Municipal sludge: 9% in 28 days

Table B.3: Fate					
					• After 43 days with previously acclimated activated inoculum, 3.75 mg/L resulted in complete mineralization
4951403, 4985135	Biodegradation	28 days	**Dose:** 90 mg/L	Readily biodegradable	**Methods:** • Test substance identified 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 DOC/L	Readily biodegradable	**Methods:** • Test substance identified as CASRN 55934-93-5 • Purity not reported • OECD Guideline 301A • GLP compliant **Results:** • Kinetic degradation results: 2% for 1 day, 9% for 3 days, 69% for 5 days, 88% for 7 days, and 96% 14 days
4985140	Biodegradation	28 days	**Doses:** 141.7 and 139 mg /L	Readily biodegradable	**Methods:** • Test substance identified as CASRN 55934-93-5 • Purity > 95% • OECD Guideline 302B • GLP compliant
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

Table B.3: Fate					
4985126	Toxicity to microorganisms	3 hours	**Doses:** 0, 10, 31.6, 100, 316, and 1000 mg/L	Negative	**Methods:** • Test substance reported as CASRN 88917-22-0 • Purity: 99.7% • OECD Guideline 209 • GLP compliant
Experimental Fate: Modelled					
Model	**Data Type**	**Endpoint**	**Predicted Endpoint**	**Notes**	
EPISuite v.4.11	Estimated	BAF	1.1	EPI Suite (Physical Property Inputs - MP = -25.2 deg C, BP = 200 deg C, VP = 0.13 mm Hg, WS = 194000 mg/L, Log K_{ow} = 0.803, Henry's Law 2.0E-07 atm-m3/mole) SMILES: CC(=O)OC(C)COC(C)COC	
EPISuite v.4.11	Estimated	BCF	3.2		
EPISuite v.4.11 (BIOWIN)	Estimated	Anaerobic biodegradation	Not predicted to biodegrade quickly under anaerobic conditions	Predicted probability of -0.1046. Fragment representation is valid. Fast degradation is defined as predicted probability >0.5.	

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Reported to the ECHA (European Chemicals Agency) database. (1998b). (2-methoxymethylethoxy)propanol: Biodegradation in water: screening tests: 006 supporting | experimental result. https://www.echa.europa.eu/web/guest/registration-dossier/-/registered-dossier/14751/5/3/2/?documentUUID=0de7e66e-7b64-444a-940d-1e5d6b3858ca

Reported to the ECHA (European Chemicals Agency) database. (2000a). 1-(2-ethoxypropoxy)propan-2-ol; 1-[(1-ethoxypropan-2-yl)oxy]propan-2-ol: Repeated dose toxicity: oral: 001 key | experimental result. https://www.echa.europa.eu/web/guest/registration-dossier/-/registered-dossier/5800/7/6/2/?documentUUID=1a294915-822a-4587-a7b4-3c17051a96ac

Reported to the ECHA (European Chemicals Agency) database. (2000b). (2-methoxymethylethoxy)propanol: genetic toxicity: in vitro: 005 key| experimental result. https://www.echa.europa.eu/web/guest/registration-dossier/-/registered-dossier/14751/7/7/2/?documentUUID=f1d01db7-8b86-4593-a2fc-f8ec1cec6de7

Reported to the ECHA (European Chemicals Agency) database. (2000c). A mixture of RR and RS isomers of: (2-(2-methoxy-1-methyl)ethoxy)-1-methylethyl acetate; (2-(2-methoxy-2-methyl)ethoxy)-1-methylethyl acetate; (2-(2-methoxy-2-methyl)ethoxy)-2-methylethyl acetate; (2-(2-methoxy-1-methyl)ethoxy)-2-methylethyl acetate: biodegradation in water: screening tests: 004 supporting | experimental result. https://echa.europa.eu/registration-dossier/-/registered-dossier/15979/5/3/2/?documentUUID=0babaf6f-5aab-4456-a17d-5941691b9a3e

Reported to the ECHA (European Chemicals Agency) database. (2000c). A mixture of RR and RS isomers of: (2-(2-methoxy-1-methyl)ethoxy)-1-methylethyl acetate; (2-(2-methoxy-2-methyl)ethoxy)-1-methylethyl acetate; (2-(2-methoxy-2-methyl)ethoxy)-2-methylethyl acetate; (2-(2-methoxy-1-methyl)ethoxy)-2-methylethyl acetate: Toxicity to aquatic algae and cyanobacteria: 001 Key | experimental result. https://echa.europa.eu/registration-dossier/-/registered-dossier/15979/6/2/6/?documentUUID=e7359564-a568-4c2f-ae39-e6b106bd7046

Reported to the ECHA (European Chemicals Agency) database. (2000d). A mixture of RR and RS isomers of: (2-(2-methoxy-1-methyl)ethoxy)-1-methylethyl acetate; (2-(2-methoxy-2-methyl)ethoxy)-1-methylethyl acetate; (2-(2-methoxy-2-methyl)ethoxy)-2-methylethyl acetate; (2-(2-methoxy-1-methyl)ethoxy)-2-methylethyl acetate: toxicity to microorganisms: 001 key | experimental result. https://echa.europa.eu/registration-dossier/-/registered-dossier/15979/6/2/8/?documentUUID=954229ee-b27c-424f-a6b5-08def6b94873

Reported to the ECHA (European Chemicals Agency) database. (2002). [(butoxymethylethoxy)methylethoxy]propan-1-ol: biodegradation in water: screening tests: 002 supporting | experimental result. https://echa.europa.eu/registration-dossier/-/registered-dossier/13383/5/3/2/?documentUUID=6371f16d-8153-4093-aef3-14f81b8624df

Fairhurst, S; Knight, R; Marrs, TC; Scawin, JW; Spurlock, MS; Swanston, DW. (1989). Percutaneous toxicity of ethylene glycol monomethyl ether and of dipropylene glycol monomethyl ether in the rat. Toxicology 57: 209-215. http://dx.doi.org/10.1016/0300-483X(89)90166-2

Landry, TD; Yano, BL. (1984). Dipropylene glycol monomethyl ether: A 13-week inhalation toxicity study in rats and rabbits. Fundam Appl Toxicol 4: 612-617. http://dx.doi.org/10.1016/0272-0590(84)90051-4

OECD (Organisation for Economic Co-operation and Development). (2003). Propylene glycol ethers: SIDS initial assessment report for SIAM 17: Arona, Italy, 11-14 November 2003. (SIDS Initial Assessment Meeting (SIAM) 17). UNEP Publications. http://www.inchem.org/documents/sids/sids/pges.pdf

Robinson, V; Bergfeld, WF; Belsito, DV; Klaassen, CD; Marks, JG; Shank, RC; Slaga, TJ; Snyder, PW; Panel, CIRE; Andersen, FA. (2009). Final report on the safety assessment of PPG-2 methyl ether, PPG-3 methyl ether, and PPG-2 methyl ether acetate. Int J Toxicol 28: 162S-174S. http://dx.doi.org/10.1177/1091581809350933

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

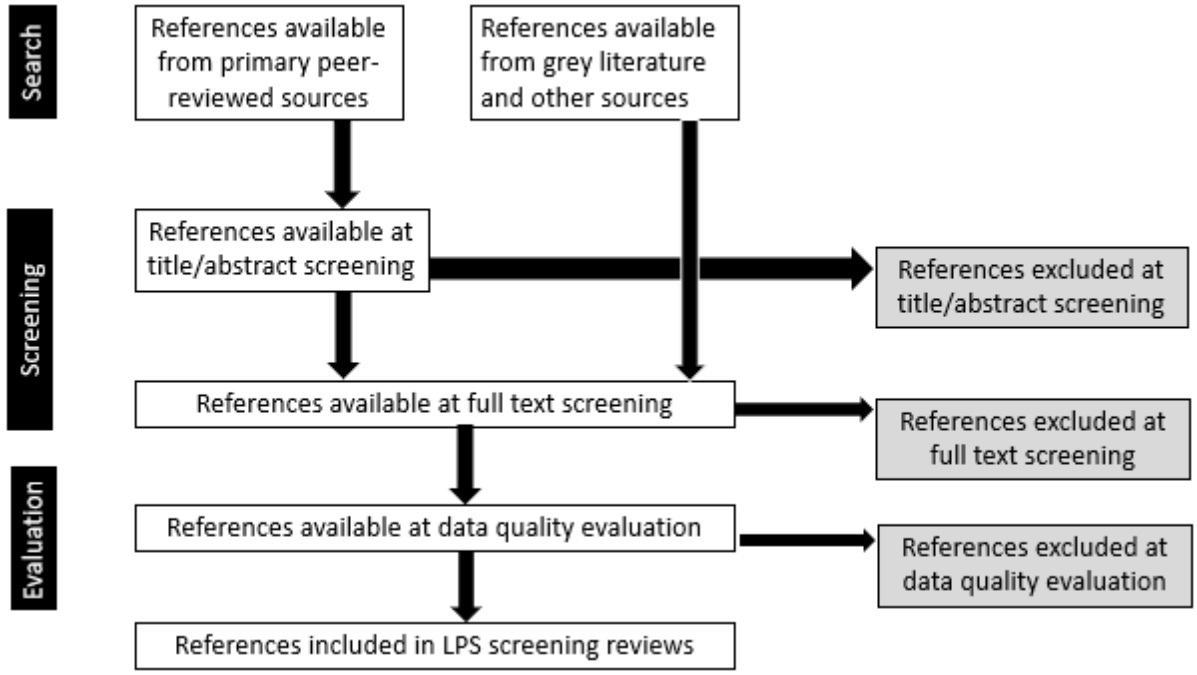
Appendix C: Literature Search Outcomes

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 dipropylene glycol methyl ether acetate. Search outcomes and reference details are provided on the candidate's HERO[53] project page.

EPA created a fit-for-purpose process to transparently document the literature search and review[54] of available hazard and fate information for low-priority substance (LPS) candidates. References from peer-reviewed primary sources, grey sources,[55] 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, dipropylene glycol methyl ether acetate, the following analogs were used for designation: dipropylene glycol, monoethyl ether (CASRN 30025-38-8); dipropylene glycol, ethyl ether (CASRN 15764-24-6); dipropylene glycol, methyl ether (CASRN 34590-

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

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

[55] 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.

94-8); dipropylene glycol, monobutyl ether (CASRN 29911-28-2); tripropylene glycol, monomethyl ether (CASRN 25498-49-1); and tripropylene glycol methyl ether (CASRN 20324-33-8). 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 dipropylene glycol methyl ether acetate 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 dipropylene glycol methyl ether acetate described above.[54] EPA also used read-across from the LPS candidate, Tripropylene glycol n-butyl ether (CASRN 55934-93-5). 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.europa.eu/web/guest/information-on-chemicals/registered-substances
ECOTOX	https://cfpub.epa.gov/ecotox/quick_query.htm
EPA – ChemView (incl. TSCATS, RBP/HC, and HPV/HPVIS)	https://chemview.epa.gov/chemview
European Food Safety Authority (EFSA)	http://www.efsa.europa.eu/
FDA	https://www.fda.gov/default.htm
HERA	http://www.heraproject.com/RiskAssessment.cfm
NICNAS	http://www.nicnas.gov.au/
NITE (J-CHECK)	http://www.safe.nite.go.jp/jcheck/search.action?request_locale=en
NTP	https://ntpsearch.niehs.nih.gov/home
OECD/SIDS	https://hpvchemicals.oecd.org/UI/Search.aspx; http://webnet.oecd.org/hpv/ui/SponsoredChemicals.aspx

C.1.2 Search Terms and Results

EPA began the literature review process for the hazard screening of dipropylene glycol methyl ether acetate 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 dipropylene glycol methyl ether acetate. 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[56]**
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-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)

[56] 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**[56]
		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 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 (DPMA; tripropylene glycol n-butyl ether)	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"
Analog 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 were returned by all search efforts across peer-reviewed databases and grey literature sources. The total number of references include database results, additional strategies, and analog searches. All references from the search efforts were screened and evaluated through the LPS literature search and review process.[54] Of these, 48 references were included for data evaluation and used to support the designation of dipropylene glycol methyl ether acetate 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 dipropylene glycol methyl ether acetate. 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[54] 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 dipropylene glycol methyl ether acetate, EPA excluded a total of 46 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[57] 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 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

[57] 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)**
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.
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[58]	5015178 5015978
The following questions apply to MECHANISTIC/ALTERNATIVE TEST METHODS evidence only		
Does the reference report a negative control that is a vehicle control or no treatment control?	No	N/A.
Does the reference report an exposure to the test substance only	No	N/A.

[58] 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)**
(i.e. no mixtures with the exception of aqueous solutions and reasonable impurities and byproducts)?		
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
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

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 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	4956637

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)**
	result in a reasonable approximation of components.	
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** The exposure duration was not appropriate for the study type and/or outcome of interest (e.g., 24 hours exposure for bacterial reverse mutation test).	N/A.
Metric 8: Test model	The test model was not reported **OR** The test model was not routinely used for evaluation of the specific outcome of interest.	N/A.
Metric 9: Outcome assessment methodology	The outcome assessment methodology was not reported. **OR**	4956637

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 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).	

C.2.2 Environmental Hazard

For the screening review of LPS candidate dipropylene glycol methyl ether acetate, 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[59] 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.									

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.

[59] 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)**
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.

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 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 dipropylene glycol methyl ether acetate, 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[60] 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.									

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

Table C.12: Screening Questions and Off-Topic References Excluded at Full Text Screening for Fate		
Question	**Off-topic if answer is:**	**References excluded (HERO ID)**
Does the reference contain information pertaining to a low-priority substance candidate?	No	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** For mixtures, the components and ratios were not characterized or did not include information that could result in a reasonable approximation of components.	N/A.
Metric 2: Study controls	The study did not include or report crucial control groups that consequently made the study unusable (e.g., no positive control for a biodegradation study reporting 0% removal). **OR** The vehicle used in the study was likely to unduly influence the study results.	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**	4956637

Table C.13: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Fate		
Data quality metric	**Unacceptable if:**	**References excluded (HERO ID)**
	The reported test concentrations were not measured, and the nominal concentrations reported greatly exceeded the substances water solubility, which would greatly inhibit meaningful interpretation of the outcomes.	
Metric 5: Testing conditions	Testing conditions were not reported, and the omission would likely have a substantial impact on study results. **OR** Testing conditions were not appropriate for the method (e.g., a biodegradation study at temperatures that inhibit the microorganisms).	N/A.
Metric 6: System type and design-partitioning	Equilibrium was not established or reported, preventing meaningful interpretation of study results. **OR** The system type and design (e.g. static, semi-static, and flow-through; sealed, open) were not capable of appropriately maintaining substance concentrations, preventing meaningful interpretation of study results.	N/A.
Metric 7: Test organism-degradation	The test organism, species, or inoculum source were not reported, preventing meaningful interpretation of the study results.	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**	N/A.

Table C.13: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Fate		
Data quality metric	**Unacceptable if:**	**References excluded (HERO ID)**
	Data indicate that disappearance or transformation of the parent compound was likely due to some other process.	
Metric 11: Confounding variables	There were sources of variability and uncertainty in the measurements and statistical techniques or between study groups.	4956637
Metric 12: Verification or plausibility of results	Reported value was completely inconsistent with reference substance data, related physical chemical properties, or otherwise implausible, suggesting that a serious study deficiency exists (identified or not).	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.[61]

For dipropylene glycol methyl ether acetate, 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
Cosmetic Ingredient Review's (CIR's) 2009 publication titled: "Final Report on the Safety Assessment of PPG-2 Methyl Ether, PPG-3 Methyl Ether, and PPG-2 Methyl Ether Acetate	2530089	This review article was part of EPA's literature review process. Each study was evaluated based on the literature search and review process described in Appendix C.

[61] Docket number EPA-HQ-OPPT-2019-0131 includes the list of 20 chemical substances that are candidates for designation as Low-Priority Substances (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-2019-0121 addresses dipropylene glycol methyl ether acetate.