Supporting Information for Low-Priority Substance 1-Butanol, 3-Methoxy-, 1-Acetate (CASRN 4435-53-4) (3-Methoxybutyl Acetate) *Final Designation*

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1. Introduction

The Lautenberg amendments to the Toxic Substances Control Act (TSCA) require EPA to designate chemical substances as either High-Priority Substances for risk evaluation, or Low-Priority Substances for which risk evaluations are not warranted at this time (section 6(b)(1)(B) and implementing regulations (40 CFR 702.3)). A high-priority substance is defined as a chemical substance that the Administrator concludes, without consideration of costs or other non-risk factors, may present an unreasonable risk of injury to health or the environment because of a potential hazard and a potential route of exposure under the conditions of use, including an unreasonable risk to potentially exposed or susceptible subpopulations identified as relevant by the Administrator. If the Administrator concludes, based on information sufficient to establish, without consideration of costs or other non-risk factors, that the high-priority standard is not met, then the substance must be designated as a low-priority substance. 1-Butanol, 3-methoxy-, 1-acetate, referenced as 3-methoxybutyl acetate 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 3-methoxybutyl acetate as a low-priority substance. EPA has also prepared a general response to comments and, as applicable, chemical-specific responses to comments.

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

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

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

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

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

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

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

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

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

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

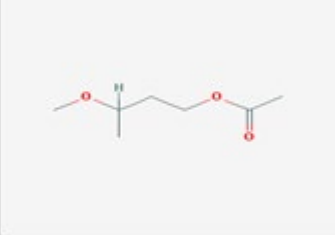
- *Appendix A (Conditions of Use Characterization):* This appendix contains a comprehensive list of TSCA and non-TSCA uses for the chemical substance from publicly available databases.

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

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

2. Background on 3-Methoxybutyl Acetate

Table 1 below provides the CAS number, synonyms, and other information on 3-methoxybutyl acetate.

Table 1: 3-Methoxybutyl Acetate at a Glance	
Chemical Name	3-Methoxybutyl Acetate
CASRN	4435-53-4
Synonyms	1-Butanol, 3-methoxy-, 1-acetate; 1-Butanol, 3-methoxy-, acetate; 3-Methoxy-1-butanol, acetate; 3-Methoxy-1-butyl acetate; 3-Methoxybutyl acetate; 3-Methoxybutylester kyseliny octove; 3-methoxy-n-butylacetat; Acetic acid 3-methoxybutyl; Acetic Acid 3-Methoxybutyl Ester; Methyl-1,3-butylene glycol acetate; 5-methoxyhexanoate
Trade Name(s)	Butoxyl
Molecular Formula	$C_7H_{14}O_3$
Representative Structure	

3-Methoxybutyl acetate is an organic chemical compound that contains both an ester functional group, which is a pair of alkyl groups connecting by a carbonyl and a linking oxygen atom (RCOOR), and an ether functional group, which is an oxygen atom connected two alkyl groups (R-O-R). Shorter chain ethers and esters typically function as solvents, which are liquids capable of dissolving other substances. 3-Methoxybutyl acetate is water soluble and miscible with common organic solvents. These properties make 3-methoxybutyl acetate ideal for use as a solvent 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 3-methoxybutyl acetate. 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 3-Methoxybutyl Acetate

Source/ Model	Data Type	Endpoint	Endpoint value	Notes
PubChem 2019	Experimental	State at room temperature	Liquid	
EPISuite v.4.11[4]	Experimental	Molecular Weight	146 g/mol	
EPISuite v.4.11	Calculated	Molecular Weight	146.19 g/mol	
Lyman et al. 1990	Estimation	Molar Volume	187 cm^3/mol	
EPISuite v.4.11	Experimental	Water Solubility	4600 mg/L	
Reported to the ECHA database, 2018	Experimental	Water Solubility	60680 - 30000 mg/L	
EPISuite v.4.11	Estimated	Water Solubility	10870 mg/L	• Kow method
Reported to the ECHA database, 2018	Experimental	Water Solubility	$4.16x10^{-1}$ mol/L	
EPISuite v.4.11	Experimental	Water Solubility	$3.15x10^{-2}$ mol/L	
EPISuite v.4.11	Estimated	Log K_{ow}	1.01	
EPISuite v.4.11	Estimated	Log K_{oa}	4.72	
EPISuite v.4.11	Estimated	Log K_{oc}	1 (MCI); 1.33 (K_{ow})	
Reported to the ECHA database, 2018	Experimental	Vapor Pressure	0.44 mm Hg at 25°C	• Converted from 58 Pa at 25°C measured according to OECD 104
EPISuite v.4.11	Estimated	Vapor Pressure	2.77 mm Hg	
EPISuite v.4.11	Estimated	Henry's Law	$1.40x10^{-6}$ atm-m^3/mol	
EPISuite v.4.11	Estimated	Volatilization	21 days (river) 23 days (lake)	
EPISuite v.4.11	Estimated	Photolysis (Indirect)	6.81 hours ($T_{1/2}$)	• OH rate constant 1.88E-11 cm^3/molecules-second (12 hour day; 1.5E6 OH/cm^3)

[4] Physical Property Inputs – Vapor Pressure = 0.44 mm Hg, Water Solubility = 60680 mg/L) SMILES: O=C(OCCC(OC)C)C

Table 2: Physical-Chemical Properties for 3-Methoxybutyl Acetate				
Source/ Model	**Data Type**	**Endpoint**	**Endpoint value**	**Notes**
				• No ozone reaction estimation
EPISuite v.4.11	Estimated	Hydrolysis	2 years at pH 7 78 days at pH 8	• Aqueous Base/Acid-Catalyzed Hydrolysis (25 deg C)
EPISuite v.4.11	Estimated	Biodegradation potential	Ready prediction: Yes	
EPISuite v.4.11	Estimated	Wastewater treatment plant removal	93.5% Total Removal (93.2% biodegradation, 0.3% sludge, 0% air)	Input parameters: BIOP = 4, BioA = 1 and BioS = 1 based on readily biodegradable (100%) met 10-day window criteria according to OECD 301E study results
EPISuite v.4.11	Estimated	BAF	1.29	
EPISuite v.4.11	Estimated	BCF	2.15	Based on regression equation

EPA's Sustainable Futures/P2 Framework Manual[5] was used to interpret the physical-chemical properties provided in Table 2. Based on its reported physical state (PubChem, 2019), 3-methoxybutyl acetate is a liquid at ambient temperature. Liquids have the potential for exposure via direct dermal contact with the substance, ingestion, or by inhalation of aerosols if they are generated. Based on its measured vapor pressure (Reported to the ECHA database, 2018), 3-methoxybutyl acetate in its pure form is expected to be volatile at ambient temperatures. As a result, exposure to 3-methoxybutyl acetate is possible through inhalation of vapors and aerosols if they are generated. In addition, its estimated Henry's law constant (EPISuite, 2019) shows that 3-methoxybutyl acetate may also volatilize slowly from water and aqueous solutions, which can also result in inhalation exposure to the vaporized compound. Based on measured water solubility (Reported to the ECHA database, 2018), 3-methoxybutyl acetate is considered water soluble. Water soluble substances have an increased potential absorption through the lungs; therefore, if inhalation of vapors or aerosols occurs, absorption through the lungs is likely. Based on its water solubility and low K_{ow} (Reported to the ECHA database, 2018), 3-methoxybutyl acetate has the potential to be moderately absorbed through the gastrointestinal tract. However, sequestration in fatty tissues is not likely based on its estimated Log K_{ow}, bioconcentration factor (BCF) and bioaccumulation factor (BAF) (EPISuite, 2019). The estimated K_{OC} (EPISuite, 2019) indicates 3-methoxybutyl acetate is highly mobile in soil, which suggests a potential to contaminate groundwater, including well water. Concern for presence in drinking water is reduced in part by 3-methoxybutyl acetate's biodegradation (discussed in Section 6.3.1). Experimental biodegradation data show that 3-methoxybutyl acetate is readily biodegradable, meaning that it has the potential to break down in the environment into carbon dioxide and water.

3.1 References

European Chemicals Agency (ECHA). (2019). 3-methoxybutyl acetate. Retrieved from https://echa.europa.eu/substance-information/-/substanceinfo/100.022.405

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

PubChem. (2019) 3-methoxybutyl acetate. Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/20498

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

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

4. Relevant Assessment History

EPA assessed the toxicological profile of 3-methoxybutyl acetate and added the chemical to the Safer Choice Program's Safer Chemical Ingredients List (SCIL) in September 2016 under the functional class of solvents. The SCIL[6] is a continuously updated list of chemicals that meet low-concern Safer Choice criteria.[7]

EPA also reviewed international assessments of 3-methoxybutyl acetate. EPA identified assessments by Canadian, Finnish, Japanese, German, and New Zealand government agencies.

The Canadian Government, through an assessment of toxicity and exposure as part of its categorization of the Domestic Substance List, found that 3-methoxybutyl acetate did not meet its criteria for further attention.[8]

The Finnish Environment Institute (SYKE)'s data bank of environmental properties of chemicals identifies 3-methoxybutyl acetate as "confirmed to be readily biodegradable."[9]

Japan's National Institute of Technology and Evaluation (NITE) categorized 3-methoxybutyl acetate as hazard class 4 for human health in 2017, the lowest-concern hazard ranking that NITE assigns.[10]

The German Environment Agency (UBA) designated 3-methoxybutyl acetate as "low hazard to waters" in August 2017 based on an assessment of ecotoxicity and environmental fate.[11]

New Zealand's Environmental Protection Authority lists 3-methoxybutyl acetate in its Chemical Classification and Information Database (CCID), which includes hazard and physical information about single chemicals for use in hazard classifications and safety information. It has classification descriptions: "acutely toxic;" "slightly harmful in the aquatic environment or are otherwise designed for biocidal action;" rapidly degradable; and not bioaccumulative.[12] Sections 6.1.2 and 6.2 of this dossier contain a summary of the reasonably available hazard information on these endpoints and an explanation of why EPA has found that acute mammalian toxicity and aquatic toxicity are not a concern for this chemical.

[6] https://www.epa.gov/saferchoice/safer-ingredients

[7] https://www.epa.gov/sites/production/files/2013-12/documents/dfe_master_criteria_safer_ingredients_v2_1.pdf

[8] https://canadachemicals.oecd.org/ChemicalDetails.aspx?ChemicalID=614DB9CA-FFD6-46F5-8ADB-DEEFF297FB4A

[9] http://wwwp.ymparisto.fi/scripts/Kemrek/Kemrek_uk.asp?Method=MAKECHEMdetailsform&txtChemId=2188

[10] http://www.safe.nite.go.jp/jcheck//direct.action?TYPE=DPAGE1&CAS=4435-53-4&MITI=2-739

[11] https://webrigoletto.uba.de/rigoletto/public/searchDetail.do?kennummer=5020

[12] https://www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/1496

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 3-methoxybutyl acetate (Appendix A) to inform which uses would be determined conditions of use.[13] 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, 3-methoxybutyl acetate is manufactured domestically and imported. No processing uses were reported to CDR. Industrial, commercial, and consumer uses include absorbents and adsorbents, fixing agents, food contact coatings, odor agents, and surface treatments. Additional consumer uses include anti-freeze and de-icing products; cleaning and washing agents; dyes/pigments; paints and coatings, among others. Based on the known manufacturing processes and uses of this chemical substance, EPA assumes distribution in commerce. According to CDR, one facility withheld recycling information. No other information is available to indicate that recycling is taking place. No information on disposal is found in CDR or through EPA's Toxics Release Inventory (TRI) Program[14] since 3-methoxybutyl acetate 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[15] and consumer uses. This research improved the Agency's understanding of the conditions of use for 3-methoxybutyl acetate. Although EPA identified uses of 3-methoxybutyl acetate 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 3-methoxybutyl acetate 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).

[13] 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).

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

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

Table 3: Conditions of Use for 3-Methoxybutyl Acetate			
Life Cycle Stage	**Category**	**Subcategory of Use**	**Source**
Manufacturing	Domestic manufacture	Domestic Manufacture – information on whether manufactured or import was not reported.	EPA (2017b)
	Import	Import- Manufacture – information on whether manufactured or import was not reported.	
Processing	Solvents (which become part of product formulation or mixture)	Printing ink manufacturing	SPIN (2018c), SPIN (2018a), SPIN (2018b), Mimaki Engineering Co., Ltd. (2018)
	Other	Chemical product and preparation manufacturing; fabricated metal product manufacturing; manufacture of furniture; transportation equipment manufacturing; manufacture, repair, and installation of machinery and equipment; miscellaneous manufacture.	SPIN (2018b), SPIN (2018a), SPIN(2018c), SPIN (2018c), Svendsen et al. (2004)
	Recycling	Recycling	EPA (2017b)[16]
Distribution	Distribution	Distribution	EPA (2017b)
Industrial Uses	Solvents (unknown)		SPIN (2018d), Celanese Corporation (2018), Celanese Corporation (2015)
	Process regulator, stabilizer, inhibitor		SPIN (2018d), (2018c)
	Reprographic agent		SPIN (2018d), CPCat (2019)
	Other	Construction; wholesale and retail trade and repair of motor vehicles and motorcycles	SPIN (2018b), SPIN (2018a), SPIN(2018c), SPIN (2018c)
Industrial/ commercial/	Solvents (which become part of product formulation or mixture)	Adhesives and sealants (Two-component glues and adhesives)	SPIN (2018d), Reported to the ECHA database, 2018a, Henkel Corporation (2013), Celanese Corporation (2011)

[16] In the 2016 CDR, one facility withheld recycling information (EPA U.S. Environmental Protection Agency (EPA). (2017). "Non-Confidential 2016 Chemical Data Reporting (CDR)." from https://www.epa.gov/chemical-data-reporting.).

Table 3: Conditions of Use for 3-Methoxybutyl Acetate			
Life Cycle Stage	**Category**	**Subcategory of Use**	**Source**
consumer uses	Other	Absorbents and adsorbents, fixing agents, food contact coatings, odor agents, surface treatment	SPIN (2018d), Synapse Information Resources (n.d.), CPCat (2019), SPIN (2018b), Reported to the ECHA database, 2018a
Consumer uses	Anti-freeze and de-icing products		Reported to the ECHA database, 2018a
	Cleaning and washing agents		SPIN (2018d)
	Dyes/Pigments		SPIN (2018d), SPIN (2018c), Reported to the ECHA database, 2018a
	Fillers		SPIN (2018d); Reported to the ECHA database, 2018a
	Paints and Coatings		New Jersey Department of Health (2009), SPIN (2018d), SPIN (2018c), Reported to the ECHA database, 2018a, Synapse Information Resources (n.d.), Celanese Corporation (2018)
	Other		Reported to the ECHA database, 2018a
Disposal	Releases to air, wastewater, solid and liquid wastes		Though not explicitly identified, releases from disposal were assumed to be reasonably foreseen[17]

[17] 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[18] 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 3-methoxybutyl acetate against the endpoints listed below. EPA's New Chemicals Program has used these endpoints for decades to evaluate chemical substances under TSCA[19] 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[20] 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[21]	**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

[18] 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.

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

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

[21] 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)[22]		**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[23]		**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[24]	**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		

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

[23] 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).

[24] 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				
		germ cells of humans or animals.		
Carcinogenicity[25]	**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[26] evidence in humans)	Negative studies or robust mechanism-based SAR
Sensitization[27]		**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[28]	**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

[25] 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).

[26] 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.

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

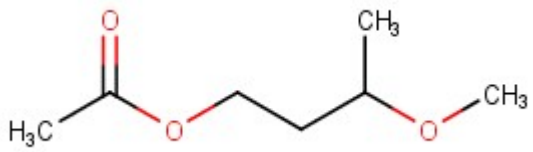
[28] Criteria derived from the Office of Pesticide Programs Acute Toxicity Categories (US EPA. *Label Review Manual.* 2010).

Table 4: Low concern Criteria for Human Health and Environmental Fate and Effects			
Environmental Fate and Effects			
Acute Aquatic Toxicity Value (L/E/IC50)[29]	**Chronic Aquatic Toxicity Value (L/E/IC50)[29]**	**Persistence (Measured in terms of level of biodegradation)[30]**	**Bioaccumulation Potential[31]**
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 3-methoxybutyl acetate. 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 3-methoxybutyl acetate. Appendix B contains more information on each study.

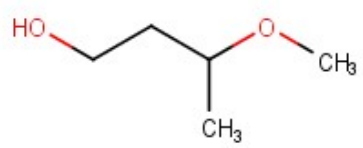
EPA used best professional judgement to select an analog for 3-methoxybutyl acetate based on similarity in structure, physical-chemical properties, and functionality, with the assumption that this chemical will have similar environmental transport and persistence characteristics, and bioavailability and toxicity profiles. 3-Methoxybutyl acetate is the acetate ester of 3-methoxybutanol. Therefore, 3-methoxybutanol is the expected alcohol metabolite of 3-methoxybutyl acetate and the biologically active metabolite *in vivo*. EPA determined 3-methoxybutanol (Table 5) to be the best analog for 3-methoxybutyl acetate in accordance with the best available science.

Table 5: 3-Methoxybutyl Acetate and Analog Structures		
CASRN	**Name**	**Structure**
4435-53-4	**3-Methoxybutyl acetate**	

[29] 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).*

[30] 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)*.

[31] 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: 3-Methoxybutyl Acetate and Analog Structures		
CASRN	**Name**	**Structure**
2517-43-3	**3-Methoxybutanol**	

6.1.1 Absorption, Distribution, Metabolism, and Excretion

To review absorption, distribution, metabolism and excretion (ADME) endpoints without adequate quality[32] experimental data, EPA used widely accepted new approach methodologies (NAMs), such as modeling and estimation tools often based on physical-chemical properties, which provided information sufficient to fill these endpoints.

Absorption

Based on the chemical's high water solubility (Section 3), there is an increased potential for absorption through the lungs from inhalation exposure. If oral ingestion occurs, moderate absorption through the gastrointestinal tract is expected. Due to its log K_{ow} (Section 3), dermal absorption is expected to be poor to moderate.

Distribution

Because 3-methoxybutyl acetate is considered water soluble (Section 3), it is likely to be distributed mainly in aqueous compartments in an organism. Based on its low log K_{ow} (Section 3), absorption and sequestration in fatty tissues is unlikely.

Metabolism

Experimental data determined to be of adequate quality[32] on 3-methoxybutyl acetate metabolite formation were not reasonably available for the assessment of metabolism. The Quantitative Structure-Activity Relationship (QSAR) toolbox[33] 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 3-methoxybutyl acetate metabolites. The predicted metabolites included carboxylic acid/ether, aldehyde/ether, alcohol/ether, and C2 carboxylic acid. A C1 aldehyde, ester/ketone, carboxylic acid/alcohol, aldehyde/alcohol, diol, ester/alcohol, and a C1 carboxylic acid were also identified as possible metabolites.

Excretion

Due to the chemical's low molecular weight and water solubility (Section 3), 3-methoxybutyl acetate is expected to be mainly excreted via urine. 3-methoxybutyl acetate may also be excreted via feces and respirable air.

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

6.1.2 Acute Toxicity

EPA assessed the potential for mammalian toxicity from acute exposures to 3-methoxybutyl acetate using experimental data and read-across from 3-methoxybutanol. A study on mice exposed to a single dose of 3-methoxybutyl acetate orally reported no mortalities at the highest tested dose (1000 mg/kg), resulting in an LD_{50} greater than 1000 mg/kg (Reported to the ECHA database, 1930). EPA also considered read-across from an analog because of the limited dose range in acute oral study on 3-methoxybutyl acetate. In an OECD Guideline 401 study, rats exposed to a single dose of 3-methoxybutanol via oral gavage demonstrated no adverse effects at that dose (2000 mg/kg), resulting in an LD_{50} greater than 2000 mg/kg (Reported to the ECHA database, 1991a). Another study on mice exposed to 3-methoxybutanol via oral gavage reported an LD_{50} of 3000 mg/kg, with the 95% confidence interval between 2400 and 3700 mg/kg (Reported to the ECHA database, 1966). Note that, as described in section 4 of this report, New Zealand made findings for this chemical based on a study that identified an LD_{50} of 4310 mg/kg. All of these studies, including the study identified by New Zealand, provide sufficient information to indicate low concern for acute toxicity with LD_{50}s expected to be greater than the low-concern benchmark of 2000 mg/kg.

6.1.3 Repeated Dose Toxicity

EPA assessed the potential for mammalian toxicity from repeated exposures to 3-methoxybutyl acetate using experimental data. A study on rats exposed to 3-methoxybutyl acetate via oral gavage for 28 days had a no observed adverse effect level (NOAEL) of 300 mg/kg-day and a lowest observed adverse effect level (LOAEL) of 1000 mg/kg-day based on abnormal respiration (J-CHECK, 2004). This result provides sufficient information to indicate low concern for toxicity from repeated oral exposures because the NOAEL and LOAEL meet the low-concern criteria benchmark of 300 mg/kg-day for a ~30-day repeated dose study.

To review the potential for inhalation and dermal repeated dose toxicity for 3-methoxybutyl acetate, EPA used route-to-route extrapolation, which is the prediction of the amount of substance administered by one route that would produce the same responses as that obtained by a given amount of the substance administered by another route.[34] EPA performed route-to-route extrapolation using the repeated dose oral study for 3-methoxybutyl acetate that reported a LOAEL of 1000 mg/kg/day based on abnormal respiration in males. EPA notes that adverse effects were not noted on functional observation battery testing, body weight, food consumption, hematology, clinical chemistry, urinalysis, gross necropsy, and histology. Therefore, based on the weight of the scientific evidence, abnormal respiration is unlikely to be considered an adverse effect. Similarly, an oral gavage developmental study (see Section 6.1.4 below) for 3-methoxybutyl acetate reported a NOAEL of 1000 mg/kg/day, which is also the highest dose tested, with no reported effects on respiration (clinical observations and gross examinations were performed in the study). Extrapolation of the oral value of 1000 mg/kg-day (based on the NOAELs for repeat dose toxicity and developmental toxicity), with consideration of the standard respiratory volume for rats and humans, human and rat bodyweights, and percent absorption using EPA's Exposure Factors Handbook,[35] results in a prediction of inhalation toxicity observed at effects greater than 0.44 mg/m^3 and 4100 mg/kg/day for dermal toxicity (see Appendix B for calculation information). Because the dose extrapolation was performed

[34] https://echa.europa.eu/documents/10162/13632/information_requirements_r8_en.pdf/e153243a-03f0-44c5-8808-88af66223258

[35] 2011 Edition. https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=236252

on the highest dose tested, which EPA determined did not cause an adverse effect, these predicted inhalation and dermal toxicity values represent doses at which EPA does not expect adverse effects to occur. The predicted dermal values provide sufficient information to indicate low concern for repeated dermal exposure. While the inhalation value technically falls within the moderate concern benchmarks outlined in Table 4, because of the studies' dosing limitations, there is uncertainty in the dose level at which adverse effects may occur following repeated inhalation exposures. This predicted inhalation value is an artifact of study dosing limitations, based on a conservative approach for route-to-route extrapolation, and does not provide evidence of moderate concern. This estimation technique provides sufficient information to screen the potential for inhalation and dermal repeated dose toxicity.

6.1.4 Reproductive and Developmental Toxicity

EPA assessed the potential for 3-methoxybutyl acetate to cause mammalian reproductive toxicity using an OECD Guideline 422 study on rats exposed via oral gavage to analog 3-methoxybutanol (BOZO, 2017a, BOZO, 2017b). Males were treated 14 days prior to mating and 28 days after mating; females were treated 14 days prior to mating and throughout pregnancy until postnatal day 4. No reproductive effects (mating, fertility, and estrus cycle) were observed at up to the highest dose tested, resulting in a NOAEL of 1000 mg/kg-day. EPA assessed the potential for mammalian developmental toxicity by 3-methoxybutyl acetate using an OECD Guideline 414 study in rats exposed via oral gavage during gestation days 7-16 (ECHA 1997b). No maternal or fetal toxicity was observed at the single dose tested (1000 mg/kg-day), resulting in a NOAEL of 1000 mg/kg-day. These results, taken with the low-concern criteria oral benchmark of 250 mg/kg-day, provide sufficient information to indicate low concern for reproductive and developmental toxicity.

6.1.5 Genotoxicity

EPA assessed the potential for 3-methoxybutyl acetate to cause genotoxicity, a potential indicator of genotoxic carcinogenicity. A bacteria reverse mutation assay in *Salmonella typhimurium* strains exposed to 3-metoxybutyl acetate reported negative results for inducing gene mutations with and without metabolic activation (Reported to the ECHA database,1992). A study on Chinese hamster lung fibroblasts exposed to 3-methoxybutyl acetate reported negative results for chromosomal aberrations with and without metabolic activation (J-CHECK 2010). EPA also considered read-across from an analog to assess the potential for 3-methoxybutyl acetate to cause genotoxicity. Mouse lymphoma cells exposed to 3-methoxybutanol were negative for gene mutations with and without metabolic activation (Reported to the ECHA database, 2010b). Additionally, human lymphocyte cells exposed to 3-methoxybutanol were negative for increased chromosomal aberrations with and without metabolic activation (Reported to the ECHA database, 2010a). These negative results provide sufficient information to indicate low concern for genotoxicity.

6.1.6 Carcinogenicity

Experimental data determined to be of adequate quality[36] on 3-methoxybutyl acetate 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

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

structure activity relationship (QSAR) models and structural alerts (SA), to assess the carcinogenic potential for 3-methoxybutyl acetate. 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.[37] For this chemical and its metabolites, there is an absence of the types of reactive structural features that are present in genotoxic carcinogens. 3-Methoxybutyl acetate is not an electrophile. ISS profiler, a QSAR model,[38] did not identify any structural alerts for 3-methoxybutyl acetate. An aldehyde was identified as a potential metabolite alert; however, this metabolite is transient and oxidized further to its Phase II metabolite(s) (see Figure 7 (metabolic tree) in the Metabolic Pathway Trees Supplemental Document[39]). Also, 3-methoxybutyl acetate goes through multiple other detoxification pathways, including ester hydrolysis and conjugation transformations that do not lead to an aldehyde metabolite. The Virtual models for property Evaluation of chemicals within a Global Architecture (VEGA) models'[40] results indicate low reliability in predicting carcinogenic potential for 3-methoxybutyl acetate. EPA determined that although the related analogs from the training set for the models are structurally similar to 3-methoxybutyl acetate, they are quite different in their functional groups,[41] which limits the model's predictability for this chemical substance.

Applying expert scientific judgement based on the reasonably available information and weight of the scientific evidence, EPA finds that 3-methoxybutyl acetate's transformation profile, lack of structural alerts in the parent chemical substance, and negative genotoxicity results provide sufficient information to indicate that this chemical is unlikely to be carcinogenic or mutagenic.

6.1.7 Neurotoxicity

While no traditional neurotoxicity studies were reasonably available for 3-methoxybutyl acetate or 3-methoxybutanol, EPA assessed the potential for neurotoxicity using relevant endpoints measured in a repeated dose study and accepted new approach methodologies (NAMs), such as predictions by U.S. EPA's ToxCast.[42]

A repeated dose study in rats exposed to 3-methoxybutyl acetate by oral gavage reported no effects on the functional observational battery (FOB) parameters examined at doses up to 1,000 mg/kg-day

[37] "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.

[38] Carcinogenicity alerts by ISS 2.4 profiler as encoded in the QSAR Toolbox 4.3 (qsartoolbox.org) and the 4 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.

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

[40] 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.

[41] For example, the training set includes analogs with strained rings that are capable of acting by a SN2 mechanism and are electrophilic (such as CASRN 3068-88-0 beta-butyrolactone or CASRN 1955-45-9 pivalolactone). These analogs are not appropriate to use to predict the carcinogenic potential of a chemical substance that has no electrophilic center and is an aliphatic ester (e.g. 3-methoxybutyl acetate).

[42] https://comptox.epa.gov/dashboard Chemical specific assay list can be found at https://comptox.epa.gov/dashboard/dsstoxdb/results?search=DTXSID2052106.

(highest dose tested) for 28 days (J-CHECK, 2004). No additional neurotoxicity-related data were available for 3-methoxybutyl acetate.

Assays related to neurological functions were identified in ToxCast[43]; however, data for 3-methoxybutyl acetate was not available for these assays.

Based on the functional observation battery results and low-hazard results for other endpoints, including, but not limited to acute toxicity and developmental toxicity, EPA has sufficient information to indicate low concern for neurotoxicity.

6.1.8 Skin Sensitization

Experimental data determined to be of adequate quality[44] on 3-methoxybutyl acetate or closely-related analogs were not reasonably available for the assessment of skin sensitization. EPA used widely accepted NAMs, such as the OECD QSAR Toolbox Version 4.2, which did not identify any structural alerts for protein binding potential of 3-methoxybutyl acetate in regard to skin sensitization. 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[45] on 3-methoxybutyl acetate or closely related analogs were not reasonably available for the assessment of respiratory sensitization potential. To model respiratory sensitization for 3-methoxybutyl acetate, EPA used NAMs, such as the QSAR Toolbox, version 4.2 models[46] for keratinocyte gene expression; protein binding potency h-CLAT; protein binding potency cysteine; protein binding potency lysine; and respiratory sensitization. No structural alerts were identified for 3-methoxybutyl acetate. The results from these NAMs and weight of the scientific evidence provide sufficient information to indicate low concern for respiratory sensitization.

6.1.10 Immunotoxicity

EPA reviewed the literature for immunotoxicity endpoints such as lymphoid organ weight, histopathology, and immune function. Specific endpoints included immune system function (e.g., T-cell dependent antibody response), immunophenotyping (e.g., changes in cell types), natural killer cell activity, host resistance assays, macrophage neutrophil function, and cell-mediated immunity

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

[44] 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

[45] 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

[46] 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

assays. Experimental data determined to be of adequate quality[47] on 3-methoxybutyl acetate or closely-related analogs were not reasonably available for the assessment of immunotoxicity potential.

Repeated dose testing is designed to be comprehensive in nature and is intended to address a wide range of possible impacts, including, but not limited to immunotoxicity. The testing required to address repeated dose toxicity typically includes routine clinical observations, hematology and clinical biochemistry, body weight/food and water consumption, as well as both gross necropsy and histopathology involving organs and organ systems. For example, repeated dose studies can evaluate changes to the spleen or thymus, which with accompanying histological changes or changes in hematological parameters can indicate potential for immunological toxicity. Where immune system-related endpoints were measured in repeated dose studies, any adverse effects would be incorporated into the lowest observed adverse effect level used against the low-concern benchmarks. Therefore, EPA relied on this information from repeated dose studies when it was reasonably available. For 3-methoxybutyl acetate and analog 3-methoxybutanol, the included repeated dose studies did not report changes in lymphoid organ weights (thymus, spleen, lymph nodes), with accompanying histopathology, or hematological changes due to exposure to this chemical substance in mammals. These results provide sufficient information to indicate low concern for immunotoxicity potential from 3-methoxybutyl acetate.

6.1.11 Skin Irritation

EPA assessed the potential for skin irritation using read-across from 3-methoxybutanol. In an OECD Guideline 404 study, rabbits exposed to 3-methoxybutanol dermally displayed slight erythema 1 hour following exposure, but this effect was fully reversed within 24 hours (Reported to the ECHA database, 1991b). Using read-across from this study, these results provide sufficient information to indicate 3-methoxybutyl acetate is low concern for skin irritation.

6.1.12 Eye Irritation

EPA assessed 3-methoxybutyl acetate's potential to act as an eye irritant using an OECD Guideline 405 study (Reported to the ECHA database, 1997a). Rabbits exposed to 3-methoxybutyl acetate experienced slight conjunctival redness and chemosis, but these effects were fully reversible in 48 hours. These results indicate moderate concern for eye irritation by 3-methoxybutyl acetate. The weight of the scientific evidence for these results is discussed in Section 8.1.

6.1.13 Hazards to Potentially Exposed or Susceptible Subpopulations

The above information supports a low human health hazard finding for 3-methoxybutyl acetate based on low-concern criteria. This finding includes considerations such as the potential for developmental toxicity and 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 3-methoxybutyl acetate.

[47] 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."

6.2 Environmental Hazard

To review environmental hazard endpoints without adequate quality[32] experimental data, EPA used widely accepted new approach methodologies (NAMs), such as modeling and estimation tools often based on physical-chemical properties, which provided information sufficient to fill these endpoints and form the basis for designation. EPA assessed environmental hazard for 3-methoxybutyl acetate based on available acute experimental data and estimated chronic toxicity values using the Ecological Structure Active Relationships (ECOSAR) Predictive Model.[48] 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 using experimental data and estimated values from ECOSAR. A study in aquatic invertebrates resulted in an LC_{50} value of 128 mg/L (Reported to the ECHA database, 1983). Predictive values from ECOSAR for aquatic vertebrates and algae were 74 mg/L and 86 mg/L, respectively. These aquatic toxicity values indicate moderate concern for acute aquatic exposure. New Zealand's Environmental Protection Agency classified this chemical as "slightly harmful in the aquatic environment or are otherwise designed for biocidal action" based on an aquatic vertebrate LC_{50} of 7.1 mg/L.[49] New Zealand's classification, discussed in Section 4, uses data that was not of sufficient quality[50] for inclusion in this analysis, based on EPA's literature review.[51] Because the toxicity values from this work are the lowest for the chemical, if EPA used them as the basis of its evaluation, this chemical would still indicate low concern for acute aquatic toxicity. For a chemical with acute aquatic toxicity values <10 ppm (mg/L) to be considered low concern for environmental hazard, the chemical must reach 60% degradation within 10 days. Given the low persistence of 3-methoxybutyl acetate (discussed in Section 6.3.1) in combination with its aquatic toxicity, EPA has sufficient information to indicate low concern for acute aquatic toxicity exposure because the aquatic toxicity data is accompanied by greater than 60% aerobic biodegradation within 10 days.

6.2.2 Chronic Aquatic Toxicity

Chronic toxicity values estimated by ECOSAR for aquatic vertebrates, aquatic invertebrates, and algae are 6.9 mg/L, 160 mg/L, and 16 mg/L, respectively. These estimations indicate moderate concern for chronic aquatic toxicity. For a chemical with chronic aquatic toxicity values <10 ppm to be considered low concern for hazard, the chemical must reach 60% degradation within 28 days as measured in an aerobic ready biodegradation test without degradation products of concern. Given the low persistence for 3-methoxybutyl acetate (discussed in 6.3.1), these predictions provide sufficient information to indicate low concern for chronic aquatic exposure, because the aquatic toxicity data is accompanied by greater than 60% aerobic biodegradation within 10 days. Aerobic biodegradation of

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

[49] https://www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/1496

[50] 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

[51] A complete list of the information needs is provided in the "Approach Document for Screening Hazard Information for Low-Priority Substances Under TSCA." This study was not included because it does not include quality experimental data (a control was not reported) as outlined in the Approach document (See HERO ID 4839256 Appendix C of this document).

3-methoxybutyl acetate (discussed in Section 6.3.1) is expected to reduce the dissolved concentration in the environment, reducing the potential for chronic exposures and aquatic toxicity.

6.3 Persistence and Bioaccumulation Potential

6.3.1 Persistence

EPA assessed environmental persistence for 3-methoxybutyl acetate using an experimental study. Based on an OECD Guideline 301E study, 95.5% of 3-methoxybutyl acetate degraded within 7 days under aerobic conditions (Reported to the ECHA database, 1995). Furthermore, 3-methoxybutanol, an analog of 3-methoxybutyl acetate, was non-toxic to microbial populations found in sewage treatment plants (Reported to the ECHA database, 2009). These results, in addition to the predicted wastewater treatment removal in Table 2, indicate 3-methoxybutyl acetate is expected to undergo extensive removal through wastewater treatment plants prior to release in the environment. These results indicate low concern for persistence in aerobic environments by readily biodegrading in less than 28 days. These results provide sufficient information to indicate low concern for persistence in aerobic environments by readily biodegrading in less than 28 days.

Anaerobic biodegradation data were not available for 3-methoxybutyl acetate or 3-methoxybutanol. Though BioWin[52] modeling did not predict this chemical to anaerobically biodegrade quickly, this chemical may still anaerobically biodegrade. The BioWin model is based on the ISO 11734 anaerobic test which measures methanogenic anaerobic biodegradation, only one of several known biodegradation pathways in anoxic environments. Other pathways include manganese and iron reduction, sulfate-reducing microorganisms, and halorespiring bacteria (Ghattas et al. 2017[53]). For 3-methoxybutyl acetate, the chemical contains degradable functional groups such as aliphatic ethers and carboxylic acids/esters. The aliphatic ether functional group anaerobically breaks down via O-demethylation by O-demethylase enzymes (Ghattas et al., 2017). Rorije et al. (2009)[54] also identified a methoxy-substituent as a potential biophore that is amenable to anerobic 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). This is a possible mechanism for 3-methoxybutyl acetate based on its structure. While EPA cannot be certain of the rates at which these anaerobic pathways may occur, this information provides further information supporting the potential for 3-methoxybutyl acetate to anaerobically biodegrade.

No degradation products of concern were identified for this chemical substance. Given the low-hazard results for mammalian toxicity, and evidence of aerobic biodegradation, EPA has sufficient information to anticipate low concern for this chemical if present in anaerobic environments.

[52] https://envirosim.com/products/biowin

[53] 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

[54] 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

6.3.2 Bioaccumulation Potential

Based on the estimated BAF value of 7.7, using the Estimation Programs Interface (EPI) Suite models,[55] EPA has sufficient information that 3-methoxybutyl acetate has low potential for bioaccumulation in the environment based on the low-concern benchmark of less than 1000.

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

7. Exposure Characterization

EPA considered reasonably available information on exposure for 3-methoxybutyl acetate. In general, there is limited information on exposure for low-hazard chemicals. EPA consulted sources of use information that include CDR and other databases and public sources. EPA used these sources (described in Table A.2) only where they augmented information from the CDR database to inform intended, known, or reasonably foreseen uses.

As shown in Tables 3 and A.3, 3-methoxybutyl acetate is a solvent with no processing uses that has 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 3-methoxybutyl acetate is based on an analysis of CDR data reported from 1986 to 2015.[56] The CDR database indicates that for reporting year 2015, companies manufactured or imported 3-methoxybutyl acetate at 16 sites. Prior to 1994, 3-methoxybutyl acetate 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 lbs. In 1994, 1998 and 2002 reporting years, aggregate production volume for 3-methoxybutyl acetate was between 10,000 and 500,000 lbs., and in 2006 and 2011, aggregate production volume was less than 500, 000 lbs. Since 2012, aggregate production volume has fallen with volumes reported at less than 100,000 lbs. with some years below 25,000 lbs.

7.2 Exposures to the Environment

EPA expects most exposures to the environment to occur during the manufacture, import, and industrial, commercial, and consumer use of 3-methoxybutyl acetate. Exposure is also possible from other uses, such as distribution and disposal. These activities could result in releases of 3-methoxybutyl acetate to media including surface water, landfills, and air.

EPA expects high levels of removal of 3-methoxybutyl acetate 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, 3-methoxybutyl acetate is expected to have low persistence (aerobic biodegradation is discussed in Section 6.3.1) and has the potential to be broken down in the environment to carbon dioxide and water. Therefore, any release of this chemical is expected to break down, reducing exposure to aquatic organisms in the water column and groundwater sources of drinking water, including well water.

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

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

If incineration releases during manufacturing occur, EPA expects significant degradation of 3-methoxybutyl acetate 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 3-methoxybutyl acetate from the potential environmental releases described above. Air exposure is unlikely from incineration. If 3-methoxybutyl acetate is present in the air from volatilization, it is expected to be reduced because of its short atmospheric half-life of 7 hours (see Table 2 in Section 3). 3-methoxybutyl acetate is unlikely to be present in surface water because it will degrade (discussed in Section 6.3.1), reducing the potential for the general population to be exposed by oral ingestion or dermal exposure. Given the low bioaccumulation or bioconcentration potential of 3-methoxybutyl acetate, oral exposure to 3-methoxybutyl acetate via fish ingestion is unlikely.

7.4 Exposures to Potentially Exposed or Susceptible Subpopulations

EPA identified workers as a potentially exposed or susceptible subpopulation based on greater exposure to 3-methoxybutyl acetate than the general population during manufacturing, processing, distribution, use, or disposal. EPA also identified consumers as a population that may experience greater exposure to 3-methoxybutyl acetate than the general population through use of anti-freeze and de-icing products; cleaning and washing agents; dyes/pigments; and paints and coatings, for example.

7.4.1 Exposures to Workers

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

7.4.2 Exposures to Consumers

Consumers may be exposed to 3-methoxybutyl acetate through the use of anti-freeze and de-icing products; cleaning and washing agents; dyes/pigments; and paints and coatings, for example. For all these uses, if dermal contact does occur, 3-methoxybutyl acetate is expected to have poor to moderate absorption through the skin based on its molecular weight, water solubility and partitioning coefficients (Section 3). If the chemical is in an aerosol product and inhalation exposure occurs, 3-methoxybutyl acetate's absorption from the lungs is likely. However, EPA expects exposure to be low since consumers will, for most uses, avoid direct contact with these types of products. 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). 3-

Methoxybutyl acetate 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 3-methoxybutyl acetate against each of the priority designation considerations in 40 CFR 702.9(a), and discussed individually in this section, under its conditions of use:

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

EPA conducted a risk-based screening-level review based on the criteria and other considerations above and other relevant information described in 40 CFR 702.9(c) to inform the determination of whether the substance meets the standard of a high-priority substance. High-priority substance means a chemical substance that EPA determines, without consideration of costs 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 3-methoxybutyl acetate. EPA used this information to inform its determination of whether 3-methoxybutyl acetate meets the statutory criteria and considerations for final designation as a low-priority substance.

- **Hazard potential:**

For 3-methoxybutyl acetate'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 3-methoxybutyl acetate is of generally low concern for human health and environmental hazard across the range of endpoints in this low-concern criteria.

- **Exposure potential:**

To understand exposure potential, EPA gathered information on physical-chemical properties, production volumes, and the types of exposures likely to be faced by workers, the general population, consumers, and children (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 populations, consumers, and workers may be exposed to 3-methoxybutyl acetate, exposure by the dermal pathway is limited by 3-methoxybutyl acetate's physical-chemical properties. If ingestion or inhalation occurs, 3-methoxybutyl acetate is expected to be metabolized and excreted, reducing the duration of exposure. If 3-methoxybutyl acetate is released into the environment, its exposure potential will be reduced through biodegradation under aerobic conditions.

Rationale: Although 3-methoxybutyl acetate may have potential to cause moderate eye irritation, the effects are reversible, thereby reducing concern for longer-term effects. TSCA conditions of use would be unlikely to result in frequent eye exposure because the use patterns do not involve intentional eye exposure. Workers could be exposed during manufacturing processes, distribution, use, and disposal through handling and splashing of solutions, or hand-to-face and eye contact. Other uses covered under TSCA, especially consumer uses in anti-freeze and de-icing products, cleaning and washing agents, and paints and coatings, would be unlikely to result in more than incidental eye exposure. Eye irritation resulting from exposure in an occupational and consumer setting is mitigated by the reversible nature of the effects and furthermore by the strong likelihood that any exposures would be self-limiting, especially by those who experience eye irritation from eye exposure.

In addition, EPA estimated repeated dose inhalation toxicity using a route-to-route extrapolation from available oral hazard data. Because the dose extrapolation was performed on the highest dose tested, which EPA determined did not cause an adverse effect, this predicted inhalation toxicity value represents a dose at which EPA does not expect an adverse effect to occur. While this value technically falls within the moderate concern benchmarks outlined in Table 4, the studies' dosing limitations do not allow EPA to determine the dose level at which adverse effects may occur following repeated inhalation exposures. In other words, any repeated dose effects from this chemical substance would be seen at doses higher than those found through the route-to-route extrapolation. The predicted inhalation value is an artifact of study dosing limitations, based on conservative approaches for the route-to-route extrapolation, and does not provide evidence of moderate concern. As part of the weight of scientific evidence, EPA notes that the Canadian Government found that 3-methoxybutyl acetate did not meet its criteria for further attention and Japan's National Institute of Technology and Evaluation (NITE) identified 3-methoxybutyl acetate as the lowest- concern hazard ranking that NITE assigns (discussed further in Section 4 of the chemical's screening review). Based on the weight of scientific evidence and reasonably available information, EPA has sufficient information that 3-methoxybutyl acetate does not meet the standard for a high-priority substance and does not consider animal testing necessary to support this finding.

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 3-methoxybutyl acetate meets the standard for a high-priority substance. The reasonably available hazard and exposure information described above provides sufficient

information to support this finding. Even if the unlikely, infrequent, and temporary occurrence of potential moderate eye irritation were to occur, EPA does not find that this potential eye irritation rises to the significance of the standard for a high-priority substance (that the substance "may present an unreasonable risk of injury to health"). Further, the route-to-route dose extrapolation for inhalation toxicity does not alter EPA's conclusion that 3-methoxybutyl acetate does not meet the standard for a high-priority substance given that this prediction represents a dose level at which EPA does not expect adverse effects to occur.

8.2. Persistence and Bioaccumulation

Approach: EPA has evaluated both the persistence and bioaccumulation potential of 3-methoxybutyl acetate 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 3-methoxybutyl acetate is biodegradable under aerobic conditions (discussed in Section 6.3.1). EPA's EPI Suite models indicate a low potential for bioaccumulation and bioconcentration (Section 6.3.2).

Conclusion: Based on an initial screen of reasonably available information on persistence and bioaccumulation, EPA concludes that the screening-level review under 40 CFR 702.9(a)(2) does not support a finding that 3-methoxybutyl acetate meets the standard for a high-priority substance. The reasonably available persistence and bioaccumulation information described above provides sufficient information to support this finding.

8.3. Potentially Exposed or Susceptible Subpopulations

Approach: TSCA Section 3(12) states that the "term 'potentially exposed or susceptible subpopulation' means a group of individuals within the general population identified by the Administrator who, due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance or mixture, such as infants, children, pregnant women, workers, consumers, or the elderly." EPA identified workers engaged in the manufacturing processes, distribution, use, and disposal of 3-methoxybutyl acetate as a potentially exposed or susceptible subpopulation (described in more detail in Section 7). Consumers are also a potentially exposed or susceptible subpopulation because of their use of products such as anti-freeze and de-icing products; cleaning and washing agents; dyes/pigments; and paints and coatings, as shown in Table 3.

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 3-methoxybutyl acetate than the general population. Because of the chemical's low-concern hazard properties and reversibility of the effects, exposure does not pose a significant increase in risk for consumers or workers.

Conclusion: Based on the Agency's understanding of the conditions of use and expected users such as potentially exposed or susceptible subpopulations, EPA concludes that the screening-level review under 40 CFR 702.9(a)(3) does not support a finding that 3-methoxybutyl acetate 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 and reversible

effects of 3-methoxybutyl acetate 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 3-methoxybutyl acetate 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, 3-methoxybutyl acetate 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, 3-methoxybutyl acetate 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 3-methoxybutyl acetate is unlikely to partition into sediment (See Section 3), predicted to biodegrade under aerobic conditions (see Section 6.3), 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, 3-methoxybutyl acetate would degrade in an aerobic environment (see Section 6). Together, these factors mean that any exposures to this chemical through drinking water sources would be short-lived, and that if ingestion were to take place, concern for adverse health effects would be low.

EPA also explored whether the chemical had been identified as a concern under U.S. environmental statutes in the past. EPA searched lists of chemicals and confirmed that 3-methoxybutyl acetate 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 3-methoxybutyl acetate under 40 CFR 702.9(a)(4) does not support a finding that 3-methoxybutyl acetate 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 3-methoxybutyl acetate and related potential exposures.

Rationale: EPA evaluated the conditions of use of 3-methoxybutyl acetate (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 3-methoxybutyl acetate'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 3-methoxybutyl acetate 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 3-methoxybutyl acetate 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 3-methoxybutyl acetate (Section 7.1) and related potential exposures (Section 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 3-methoxybutyl acetate as a low-priority substance could result in increased use and higher production volumes. EPA expects, however, that any changes in 3-methoxybutyl acetate'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 3-methoxybutyl acetate's consistently low-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 exposures, 3-methoxybutyl acetate 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 3-methoxybutyl acetate as a low-priority substance.

9. Final Designation

Based on a risk-based screening-level review of the chemical substance and relevant information received from the public and other information as appropriate and consistent with TSCA section 26(h), (i) and (j), EPA concludes that 3-methoxybutyl acetate 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 3-methoxybutyl acetate as a low-priority substance.

Appendix A: Conditions of Use Characterization

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

A.1. CDR Manufacturers and Production Volume

The Chemical Data Reporting (CDR) rule (previously known as the Inventory Update Rule, or IUR), under TSCA section 8, requires manufacturers (including importers) to report information on the chemical substances they produce domestically or import into the U.S., generally above a reporting threshold of 25,000 lb. per site per year. According to the 2016 CDR database, 1 company manufactured or imported 3-methoxybutyl acetate at 1 site for reporting year 2015. Individual production volumes were withheld, but may be available in later releases of the 2016 CDR.

Table A.1 presents the historic production volume of 3-methoxybutyl acetate from the CDR (previously known as the Inventory Update Rule, or IUR) from 1986-2015. Prior to 1994, 3-methoxybutyl acetate was not reported in the CDR. This does not mean it was not being produced or imported, but more likely that no single entity site was producing above the reporting threshold. In 1994, 1998 and 2002 reporting years, aggregate production volume for 3-methoxybutyl acetate was between 10,000 and 500,000 lbs., and in 2006 and 2011 aggregate production volume was less than 500,000 lbs. Since 2012, aggregate production volume has fallen with volumes reported at less than 100,000 lbs. with some years below 25,000 lbs.

Table A.1: 1986-2015 National Production Volume Data for 3-Methoxybutyl Acetate (Non-Confidential Production Volume in Pounds)

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

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

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

A.2. Uses

A.2.1 Methods for Uses

Section A.2 provides a list of known uses of 3-methoxybutyl acetate, organized by category of use. To compile the uses, EPA searched publicly available databases listed in Table A.2 and conducted additional internet searches to clarify uses. Search terms differed among databases because of different search term requirements for each database (i.e., some databases search by CASRN while others search by chemical name).

Table A.2: Sources Searched for Uses of 3-Methoxybutyl Acetate

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)	4435-53-4	No
Canada Chemicals Management Plan information sheets	Government of Canada (2018)	3-methoxybutyl acetate	No
Chemical and Product Categories (CPCat)	Dionisio, Frame et al. (2015)	4435-53-4	Yes
ChemView [2]	EPA ((2018))	4435-53-4	Yes
Children's Safe Product Act Reported Data	Washington State Dept. of Ecology (2018)	4435-53-4	No
Consumer Product Information Database (CPID)	DeLima Associates (2018)	4435-53-4	No
Danish surveys on chemicals in consumer products	Danish EPA (2018)	N/A, There is no search, but report titles were checked for possible information on the chemical	Yes
Datamyne	Descartes Datamyne (2018)	3-methoxybutyl acetate	No
DrugBank	DrugBank (2018)	3-methoxybutyl acetate	No
European Chemicals Agency (ECHA) Registration Dossier	ECHA ((2018))	4435-53-4	Yes
eChemPortal [2]	OECD ((2018))	4435-53-4	No
Envirofacts [2]	EPA ((2018))	4435-53-4	No
Functional Use Database (FUse)	EPA ((2017))	4435-53-4	No
Kirk-Othmer Encyclopedia of Chemical Technology	Kirk-Othmer (2006))	3-methoxybutyl acetate	No
Non-Confidential 2016 Chemical Data Reporting (CDR)	EPA ((2017))	4435-53-4	Yes
PubChem Compound	Kim, Thiessen et al. (2016)	4435-53-4	Yes
Safer Chemical Ingredients List (SCIL)	EPA ((2018))	4435-53-4	Yes
Synapse Information Resources [2]	Synapse Information Resources (2009)	3-methoxybutyl acetate	Yes

Table A.2: Sources Searched for Uses of 3-Methoxybutyl Acetate			
Title	**Author and Year**	**Search Term(s)**	**Found Use Information?** [1]
Resource Conservation and Recovery Act (RCRA)	EPA ((2018))	3-methoxybutyl acetate; butoxyl; acetate	No
Scorecard: The Pollution Information Site	GoodGuide (2011)	4435-53-4	No
Skin Deep Cosmetics Database	EWG (2018)	4435-53-4	No
Toxics Release Inventory (TRI)	EPA ((2018))	4435-53-4	No
TOXNET [2]	NLM ((2018))	4435-53-4	No
Ullmann's Encyclopedia of Industrial Chemistry	Ullmann's (2000)	3-methoxybutyl acetate	No
Additional sources identified from reasonably available information			
Celanese Corporation	Celanese Corporation (2011)	Incidentally identified while researching details of this chemical's uses and products.	Yes
Danish Technological Institute	Svendsen et al. (2004)		
Henkel Corporation	Henkel Corporation (2013)		
Mimaki Engineering Company, Ltd.	Mimaki Engineering Co. Ltd (2008)		
New Jersey Dept. of Health	New Jersey Department of Health (2009)		
Substances in Preparations in Nordic Countries (SPIN)	SPIN ((2018))		

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 1,113 patents referencing "3-methoxybutyl 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 3-methoxybutyl acetate 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 3-Methoxybutyl Acetate

Table A.3: Uses of 3-Methoxybutyl Acetate		
Use or Process	**Expected Users**	**Description of Use and References**
TSCA Conditions of Use: Industrial Uses		
Construction	Industrial	SPIN ((2018)); SPIN ((2018)) SPIN identifies use of 3-methoxybutyl acetate in construction of buildings and specialized construction activities in Denmark as recently as 2015. 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 due to inclusion in the SPIN Industry National and Industrial (NACE) databases.
Manufacture of chemicals and chemical products	Industrial	SPIN ((2018)); Reported to the ECHA database, (2018) SPIN identifies use of 3-methoxybutyl acetate in the manufacture of chemicals and chemical products in Nordic countries as recently as 2004. The ECHA registration dossier identifies use of 3-methoxybutyl acetate in the manufacture of bulk, large-scale chemicals and the manufacture of fine chemicals. 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 due to inclusion in the SPIN Industrial (NACE) database and inclusion in ECHA's uses at industrial sites.
Manufacture of fabricated metal product, except machinery and equipment	Industrial	SPIN ((2018)); SPIN ((2018)) SPIN identifies use of 3-methoxybutyl acetate in the manufacture of fabricated metal products in multiple Nordic countries as recently as 2016. 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 due to inclusion in the SPIN Industry National and Industrial (NACE) databases.
Manufacture of furniture	Industrial	SPIN ((2018)) SPIN identifies use of 3-methoxybutyl acetate in the manufacture of furniture in Nordic countries as recently as 2007. 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 due to inclusion in the SPIN Industrial (NACE) database.

Table A.3: Uses of 3-Methoxybutyl Acetate		
Use or Process	**Expected Users**	**Description of Use and References**
Manufacture of motor vehicles, trailers, semi-trailers, and other transport equipment	Industrial	SPIN ((2018)) SPIN identifies use of 3-methoxybutyl acetate in the manufacture of motor vehicles and other transportation equipment in Nordic countries as recently as 2015. 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 due to inclusion in the SPIN Industrial (NACE) database.
Manufacture, repair, and installation of machinery and equipment	Industrial	SPIN ((2018)) SPIN identifies use of 3-methoxybutyl acetate in the manufacture, repair, and installation of machinery and equipment in Nordic countries as recently as 2011. 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 due to inclusion in the SPIN Industrial (NACE) database.
Wholesale and retail trade and repair of motor vehicles and motorcycles	Industrial	SPIN ((2018)); SPIN ((2018)) SPIN identifies use of 3-methoxybutyl acetate in wholesale and retail trade and repair of motor vehicles and motorcycles and in automotive painting in multiple Nordic countries as recently as 2016. 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 due to inclusion in the SPIN Industry National and Industrial (NACE) databases.
TSCA Conditions of Use: Personal Care Products		
Toothbrushes	Consumer	Svendsen et al. (2004) A report by the Danish Technological Institute identified use of 3-methoxybutyl acetate in toothbrushes. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. No current products containing 3-methoxybutyl acetate could be found. This report is a survey of chemical substances found in consumer products; therefore, the expected users are consumer.

Table A.3: Uses of 3-Methoxybutyl Acetate		
Use or Process	**Expected Users**	**Description of Use and References**
TSCA Conditions of Use: Miscellaneous		
Absorbents and adsorbents	Industrial, commercial, consumer uses	SPIN ((2018)) SPIN identifies use of 3-methoxybutyl acetate in absorbents and adsorbents in Finland as recently as 2002. 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 industrial, commercial, and consumer.
Adhesives, binding agents	Consumer, unknown	SPIN ((2018)); Reported to the ECHA database, (2018); Henkel Corporation (2013); Celanese Corporation (2011) Celanese Corporation identifies use of 3-methoxybutyl acetate as a solvent in isocyanate and epoxy containing systems. The Henkel Corporation provides a SDS for an adhesive product that contains 3-methoxybutyl acetate. SPIN reports use of 3-methoxybutyl acetate in adhesives, binding agents, binding materials, and adhesives based on organic thinners in multiple Nordic countries as recently as 2015. The ECHA registration dossier also identifies 3-methoxybutyl acetate as an ingredient in adhesives and sealants in European countries. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are consumer due to ECHA's inclusion in consumer uses. Other expected users are unknown, due to the limited availability of information.
Anti-freeze and de-icing products	Consumer	Reported to the ECHA database, (2018) The ECHA registration dossier identifies use of 3-methoxybutyl acetate in anti-freeze and de-icing products in European countries. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are consumer due to ECHA's inclusion in consumer uses.
Cleaning/washing agents	Unknown	SPIN ((2018)) SPIN identifies use of 3-methoxybutyl acetate in cleaning/washing agents in multiple Nordic countries as recently as 2015. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are unknown, due to the limited availability of information.

Table A.3: Uses of 3-Methoxybutyl Acetate		
Use or Process	**Expected Users**	**Description of Use and References**
Coloring agents	Consumer, unknown	SPIN ((2018)); SPIN ((2018)); Reported to the ECHA database, (2018) SPIN identifies use of 3-methoxybutyl acetate in coloring agents, dyestuff, pigments, and dyeing auxiliaries in Finland as recently as 2003. The ECHA registration dossier identifies use of 3-methoxybutyl acetate in textile dyes and finishing and impregnation products. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are consumer due to ECHA's inclusion in consumer uses. Other expected users are unknown, due to the limited availability of information.
Fillers	Consumer, unknown	SPIN ((2018)); Reported to the ECHA database, (2018) SPIN identifies use of 3-methoxybutyl acetate in fillers and insulation materials in multiple Nordic countries as recently as 2014. The ECHA registration dossier identifies use of 3-methoxybutyl acetate in fillers, putties, plasters and modeling clay. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are consumer due to ECHA's inclusion in consumer uses. Other expected users are unknown, due to the limited availability of information.
Fixing agents	Industrial, commercial, consumer uses	SPIN ((2018)) SPIN identifies use of 3-methoxybutyl acetate in fixing agents in Finland as recently as 2004. 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 industrial, commercial, and consumer.
Food-contact coatings	Industrial/ commercial/ consumer uses	Synapse Information Resources (2009) Synapse Information Resources reports use of 3-methoxybutyl acetate in food-contact coatings. 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 industrial, commercial, and consumer.

Table A.3: Uses of 3-Methoxybutyl Acetate		
Use or Process	**Expected Users**	**Description of Use and References**
Odor agents	Industrial/ commercial/ consumer uses	SPIN ((2018)); Dionisio, Frame et al. (2015) SPIN identifies use of 3-methoxybutyl acetate in odor agents (The International Fragrance Association (IFRA)) in Finland as recently as 2012. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are unknown, due to the limited availability of information.
Paints, lacquers, thinners, and varnishes	Consumer, unknown	New Jersey Department of Health (2009); SPIN ((2018)); SPIN ((2018)); Reported to the ECHA database, (2018); Synapse Information Resources (2009); Celanese Corporation (2018) The New Jersey Department of Health identifies use of 3-methoxybutyl acetate as a solvent in the paint and lacquer industry. Celanese Corporation sells a product, Butoxyl, which is used in brush-applied paints. SPIN identifies use of 3-methoxybutyl acetate in paints, lacquers, primers, diluents, thinners, hardeners, and varnishes in multiple Nordic countries as recently as 2016. The ECHA registration dossier also identifies 3-methoxybutyl acetate as an ingredient in coatings and paints, finger paints, thinners, and paint removers. Synapse identifies use of 3-methoxybutyl acetate in urethane coatings, and acrylic, and nitrocellulose. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are consumer due to ECHA's inclusion in consumer uses. Other expected users are unknown, due to the limited availability of information.
Polishes and wax blends	Consumer	Reported to the ECHA database, (2018) The ECHA registration dossier identifies use of 3-methoxybutyl acetate in polishes and wax blends in European countries. Expected users are consumer due to ECHA's inclusion in consumer uses.

Table A.3: Uses of 3-Methoxybutyl Acetate		
Use or Process	**Expected Users**	**Description of Use and References**
Printing inks	Industrial, unknown	SPIN ((2018)); SPIN ((2018)); SPIN ((2018)); Mimaki Engineering Co. Ltd (2008) Mimaki Engineering identifies use of 3-methoxybutyl acetate as a solvent pigment ink in inks for ink jet printers. SPIN identifies use of 3-methoxybutyl acetate in printing inks, serigraphy inks, printing and reproduction of recorded media in multiple Nordic countries as recently as 2010. 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 due to inclusion in the SPIN Industry National and Industrial (NACE) databases. Other expected users are unknown, due to the limited availability of information.
Process regulators	Unknown	SPIN ((2018)); SPIN ((2018)) SPIN identifies use of 3-methoxybutyl acetate in process regulators, stabilizers, and inhibitors in multiple Nordic countries as recently as 2012. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are unknown, due to the limited availability of information.
Reprographic agents	Industrial	SPIN ((2018)); Dionisio, Frame et al. (2015) SPIN identifies use of 3-methoxybutyl acetate in reprographic agents (photographic) in multiple Nordic countries as recently as 2010. 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 industrial.
Solvents	Industrial	EPA ((2017)); SPIN ((2018)); Celanese Corporation (2018); Celanese Corporation (2015) CDR reports one domestic producer of 3-methoxybutyl acetate (Celanese Corporation), however, no use information was reported. Celanese Corporation sells a product in the Americas with a 99.5 percent concentration of 3-methoxybutyl acetate (Butoxyl), the primary use of which is as a solvent. SPIN identifies use of 3-methoxybutyl acetate in solvents in multiple Nordic countries as recently as 2015. 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 industrial.

Table A.3: Uses of 3-Methoxybutyl Acetate		
Use or Process	**Expected Users**	**Description of Use and References**
Surface treatment	Consumer, industrial	SPIN ((2018)); Dionisio, Frame et al. (2015); SPIN ((2018)); Reported to the ECHA database, (2018); Synapse Information Resources (2009) SPIN identifies use of 3-methoxybutyl acetate in surface treatment (fluid property modulators and protection lacquers) in multiple Nordic countries as recently as 2015. The ECHA registration dossier also identifies use of 3-methoxybutyl acetate in non-metal surface treatment products. Synapse Information Resources reports use of 3-methoxybutyl acetate in epoxy and aminoalkyl resins. No further information about this use could be found and it is unknown whether this is an ongoing use in the United States. Expected users are consumer due to ECHA's inclusion in consumer uses, and industrial due to inclusion in the SPIN Industry National database.
Children's Products No uses in products intended for children were identified, however, there is a possible consumer use in toothbrushes, which could be used by children.		
Recycling and Disposal In the 2016 CDR, one facility withheld recycling information (EPA (2017)).		

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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
4839296	Oral	Mice	Single dose	**Doses:** 100, 500, and 1000 mg/kg **Replicates:** 2 per dose	**LD_{50}** > 1000 mg/kg	**Methods:** • Substance reported as CASRN 4435-53-4 • Purity not reported • Pre-dates GLP compliant
5093123	Oral (gavage)	Wistar rats	Single dose, observed for 14 days	**Dose**: 2000 mg/kg **Replicates**: 5 per sex	**LD_{50}** > 2000 mg/kg	**Methods:** • Substance reported as CASRN 2517-43-3 • Purity: 99.5% • OECD Guideline 401 • GLP compliant
5093162	Oral (gavage)	Albino mice	Single dose, observed for 6 days	**Doses:** 1000, 2000, 4000 and 8000 mg/kg **Replicates:** 3 per dose	**LD_{50}**: 3000 mg/kg, CI between 2400 and 3700 mg/kg	**Methods:** • Substance reported as CASRN 2517-43-3 • Purity: 99.8% • Not GLP compliant **Mortality Results:** • 1/3 animal in 2000 mg/kg • 2/3 animals in 4000 mg/kg • 3/3 animals in 8000 mg/kg

Repeated Dose Toxicity

Source	Exposure Route	Species & strain (if available)	Duration	Doses and replicate number	Effect	Study Details
4839287	Oral (gavage)	Crj: CD IGS rats	28 days	**Doses**: 0, 100, 300, and 1000 mg/kg-day **Replicates**: 5 per sex per group	**NOAEL:** 300 mg/kg-day **LOAEL:** 1000 mg/kg-day; based on abnormal respiration	**Methods:** • Substance reported as CASRN 4435-53-4 • Purity: 99.8% • OECD Guideline 407 • GLP compliant **Results:** • LOAEL of 1000 mg/kg-day based on abnormal respiration in males, also increased and transient salivation observed

Table B.1: Human Health Hazard						
Reproductive Toxicity						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
5926437, 6302293	Oral (gavage)	Sprague-Dawley rats	14 days before mating plus 28 days post mating (for males) or throughout gestation until postnatal day 4 (for females)	**Doses:** 0, 100, 300 and 1000 mg/kg-day **Replicates:** 10-12 per sex per group	**NOAEL:** 1000 mg/kg-day	**Methods:** • Substance reported as CASRN 2517-43-3 • Purity: 99.7% • OECD Guideline 422 • GLP compliant • 14-day recovery period following treatment allowed for 0 and 1000 mg/kg group **Results:** • No effects on female reproductive parameters, fertility, or pregnancy
Developmental Toxicity						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
4839284	Oral (gavage)	Wistar rats	Gestational Days 7-16	**Doses:** 0 and 1000 mg/kg-day **Replicates:** 20 pregnant females per group	**NOAEL:** 1000 mg/kg-day	**Methods:** • Substance reported as CASRN 4435-53-4 • Purity: 99.7% • OECD Guideline 414 • GLP compliant **Results:** • No maternal or fetal toxicity observed
Cancer						
Source	**Effect**		**Study Details**			
Oncologic v8.0	OncoLogic currently has no assessment criteria regarding methoxy acetates		Structure could not be evaluated by Oncologic			

Table B.1: Human Health Hazard						
ISS v2.4[57]	Negative (Estimated)	**Methods:** Carcinogenicity alerts (genotoxic and non-genotoxic) by ISS profiler as available within the OECD Toolbox v4.3 **Results:** No alerts were identified for the parent structure (an aldehyde alert was identified for the aldehyde formed upon hydrolysis) (see Figure 7 metabolic tree in Metabolic Pathway Trees Supplemental Document[58]).				
VEGA 1.1.4[59]	3-Methoxybutyl acetate was processed through all 4 models. All of the models 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 (3-Methoxybutyl acetate lies outside of the applicability domain (AD) of the model) • ISS 1.0.2: Low reliability (3-Methoxybutyl acetate lies outside of the AD) • IRFMN/Antares 1.0.0: Low reliability (3-Methoxybutyl acetate lies outside of the AD) • IRFMN/ISSCAN-GX 1.0.0: Low reliability (3-Methoxybutyl acetate lies outside of the AD)				
Genotoxicity						
Source	**Test Type & endpoint**	**Species & strain (if available)**	**Metabolic activation**	**Doses and controls**	**Results**	**Study Details**
4839293,	Gene Mutation *(in vitro)*	Salmonella typhimurium strains TA 1535, 1537, 98, 100, and 1538	With and without	**Doses:** 0, 4, 20, 100, 500, 5,000 and 10,000 µg/plate	Negative	**Methods:** • Substance reported as CASRN 4435-53-4 • Purity: 99.7% • OECD Guideline 471 • GLP compliant
4839292	Chromosomal aberration (*in vitro)*	Chinese hamster lung fibroblasts	With and without	**Doses:** 0, 1.25, 2.5, 5, and 10 mM	Negative	**Methods:** • Substance reported as CASRN 4435-53-4 • Purity: 99.8%

[57] 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.

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

[59] 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						
						• GLP compliant
5924190	Gene Mutation *(in vitro)*	Mouse lymphoma L5178Y cells	With and without	**Doses:** 0.3, 1, 3, 10, 33, 100, 333, and 1042 µg/mL	Negative	**Methods:** • Substance reported as CASRN 2517-43-3 • Purity: 99.7% • OECD Guideline 476 • GLP compliant
5093961	Chromosomal aberration (*in vitro)*	Human lymphocyte cells	With and without	**Doses:** up to 1042 µg/mL	Negative	**Methods:** • Substance reported as CASRN 2517-43-3 • Purity: 99.7% • OECD Guideline 473 • GLP compliant
Neurotoxicity						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
4839287	Oral (gavage)	Crj: CD IGS rats	28 days	**Doses**: 0, 100, 300, and 1000 mg/kg-day **Replicates**: 5 per sex per group	**NOAEL:** 1000 mg/kg-day	**Methods:** • Substance reported as CASRN 4435-53-4 • Purity: 99.8% • OECD Guideline 407 • GLP compliant **Results:** • No effects on the functional observational battery (FOB) parameters
Irritation						
Source	**Exposure Route**	**Species & Strain (if available)**	**Duration**	**Doses**	**Effect**	**Study Details**
5094080	Skin	New Zealand white rabbits	4 hour exposure, observed for 72 hours	**Dose:** 0.5 mL of undiluted substance **Replicates:** 3 rabbits	Negative	**Methods:** • Substance reported as CASRN 2517-43-3 • Purity: 99.5% • OECD Guideline 404 • GLP compliant **Results:** • Slight erythema was observed at 1 hour • All effects were fully reversed within 1 day

Table B.1: Human Health Hazard						
4839281	Ocular	New Zealand white rabbits	24 hour exposure, observed for 72 hours	**Dose:** 0.1 mL of undiluted substance **Replicates:** 3 rabbits	Moderate	**Methods:** • Substance reported as CASRN 4435-53-4 • Purity: 99.7% • OECD Guideline 405 • GLP compliant **Results:** • Conjunctival Redness score was 0.6/3 and was fully reversed in 2 days • Chemosis score was 1-3/4 at 1 hour, was fully reversed in 1 day

Table B.2: Route to Route Extrapolation Information for Oral to Inhalation Exposures for 3 Methoxybutyl Acetate		
Formula[60]: Corrected inhalation NOAEL = ($NOAEL_{ORAL}$ or $LOAEL_{ORAL}$) x ($1/SRV_{rat}$) x ($ABS_{oral\text{-}rat}/ABS_{inh\text{-}human}$) x ($sRV_{human}/wRV_{human}$)		
Variable	**Units**	**Value Used**
Corrected inhalation NOAEL	Predicted NOAEL for inhalation exposure to humans, mg/m^3	0.440
$NOAEL_{ORAL}$	No observed adverse effect level from oral exposure, mg/kg-bw/day	1000
SRV_{RAT}	Rat standard respiratory volume for 8-hours, m^3/kg-bw	0.38
$ABS_{ORAL\text{-}RAT}$	Percent absorption by the oral route in rats, assuming "moderate" absorption, %	15
$ABS_{INHAL\text{-}HUMAN}$	Percent absorption by inhalation in humans, assuming "good" absorption, %	60
sRV_{HUMAN}	Human standard respiratory volume for 8-hours, m^3	6.7
wRV_{HUMAN}	Worker respiratory volume for 8-hours, m^3	10

[60] ECHA (European Chemicals Agency). 2012. *Guidance on information requirements and chemical safety assessment. Chapter R.8: Characterization of dose [concentration]-response for human health.* Available at: https://echa.europa.eu/documents/10162/13632/information_requirements_r8_en.pdf/e153243a-03f0-44c5-8808-88af66223258. See example B.3.

Table B.3: Route to Route Extrapolation Information for Oral to Dermal Exposures for 3 Methoxybutyl Acetate		
Formula[61]: Corrected dermal NOAEL = $NOAEL_{ORAL}$ × ($ABS_{ORAL\text{-}RAT}$ ÷ $ABS_{DERMAL\text{-}HUMAN}$) × ($BW_{HUMAN}$ ÷ BW_{RAT})$^{1/4}$		
Variable	**Definition and Units**	**Value Used**
Corrected dermal NOAEL	Predicted NOAEL for dermal exposure to humans, mg/kg-bw/day	4100
$NOAEL_{ORAL}$	mg/kg-bw/day	1000
$ABS_{ORAL\text{-}RAT}$	Percent absorption by the oral route in rats, assuming "moderate" absorption, %	15
$ABS_{DERMAL\text{-}HUMAN}$	Percent absorption by the dermal route in humans, assuming "poor to moderate" absorption, %	15
BW_{HUMAN}	Human bodyweight, kg	71.8
BW_{RAT}	Rat bodyweight, kg	0.25

[61] ECHA (European Chemicals Agency). 2012. *Guidance on information requirements and chemical safety assessment. Chapter R.8: Characterization of dose [concentration]-response for human health.* Available at: https://echa.europa.eu/documents/10162/13632/information_requirements_r8_en.pdf/e153243a-03f0-44c5-8808-88af66223258. See example B.5.

Table B.4: Environmental Hazard					
Aquatic Toxicity: Experimental					
Source	**Species**	**Duration**	**Doses and replicate number**	**Effect**	**Study Details**
4839253	*Chaetogammarus marinus*	96 hours	**Doses:** 0, 32,56,100, 180, 320, 560, and 1000 mg/L	**LC_{50}:** 128 mg/L	• Substance reported as CASRN 4435-53-4 • Purity not reported • EPA OPPTS 850.1020 • GLP compliance not reported
Aquatic Toxicity: Estimated					
Model	**Chemical Class**	**Species**	**Predicted Effect Level**	**Notes**	
ECOSAR v2 (Class: Esters)	Acute	Freshwater fish	**LC_{50}**: 74 mg/L	Estimated using the following experimental input value: water solubility= 4.6E+3 mg/L	
ECOSAR v2 (Class: Esters)	Acute	Daphnia magna	**LC_{50}**: 170 mg/L	Estimated using the following experimental input value: water solubility= 4.6E+3 mg/L	
ECOSAR v2 (Class: Esters)	Acute	Green algae	**EC_{50}**: 86 mg/L	Estimated using the following experimental input value: water solubility= 4.6E+3 mg/L	
ECOSAR v2 (Class: Esters)	Chronic	Freshwater fish	6.9 mg/L	Estimated using the following experimental input value: water solubility= 4.6E+3 mg/L	
ECOSAR v2 (Class: Esters)	Chronic	Daphnia magna	160 mg/L	Estimated using the following experimental input value: water solubility= 4.6E+3 mg/L	
ECOSAR v2 (Class: Esters)	Chronic	Green algae	16 mg/L	Estimated using the following experimental input value: water solubility= 4.6E+3 mg/L	

Table B.5: Fate					
Environmental Fate: Experimental					
Source	**Endpoint**	**Duration**	**Doses and number of replicates**	**Results**	**Study Details**
4839258	DOC removal	28 hours	**Dose:** 30 mg/L	95.5% at day 7	**Methods:** • Substance reported as CASRN 4435-53-4 • Purity: 99.6% • OECD Guideline 301E • GLP compliant
5094143	Toxicity to microorganisms	3 hours	**Doses:** 10 to 1000 mg/L	**EC_{50}** > 1000 mg/L	**Methods:** • Substance reported as CASRN 2517-43-3 • Purity: 98.8% • OECD Guideline 209 • GLP compliant
Environmental Fate: Modelled					
Model	**Data Type**	**Endpoint**	**Predicted Endpoint**	**Notes**	
EPISuite v.4.11	Estimated	BAF	1.29		
EPISuite v.4.11	Estimated	BCF	2.15	Regression on eq	
EPISuite v. 4.11 (BIOWIN 7)	Estimated	Anaerobic biodegradation	Not predicted to biodegrade quickly under anaerobic conditions	Predicted probability of 0.3981. 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. (2009). 3-Methoxybutan-1-ol: Toxicity to microorganisms: 001 key | Experimental result. https://www.echa.europa.eu/web/guest/registration-dossier/-/registered-dossier/5155/6/2/8/?documentUUID=823b32f4-c0ea-44b4-bfc0-b170f483253b

Reported to the ECHA (European Chemicals Agency) database. (2010a). 3-Methoxybutan-1-ol: Genetic toxicity: in vitro: 001 Key | Experimental result. https://www.echa.europa.eu/web/guest/registration-dossier/-/registered-dossier/5155/7/7/2/?documentUUID=fbc5c10a-22a7-4b9b-af01-21ceaf54ec69

Reported to the ECHA (European Chemicals Agency) database. (2010b). 3-Methoxybutan-1-ol: Genetic toxicity: in vitro: 002 Key | Experimental result. https://echa.europa.eu/registration-dossier/-/registered-dossier/5155/7/7/2/?documentUUID=948261b3-1d0d-4670-a20e-698be4a82524

J-CHECK (Japanese CHEmical Collaborative Knowledge database). (2004). #67: Repeated dose toxicity: oral: subacute [CASRN 4435-53-4]. Available online at http://www.safe.nite.go.jp/jcheck/template.action?ano=26691&mno=2-0739&cno=4435-53-4&request_locale=en

J-CHECK (Japanese CHEmical Collaborative Knowledge database). (2010). #70: Genetic toxicity in vitro: chromosome aberration: in vitro mammalian chromosome aberration test [CASRN 4435-53-4]. Available online at http://www.safe.nite.go.jp/jcheck/template.action?ano=26753&mno=2-0739&cno=4435-53-4&request_locale=en

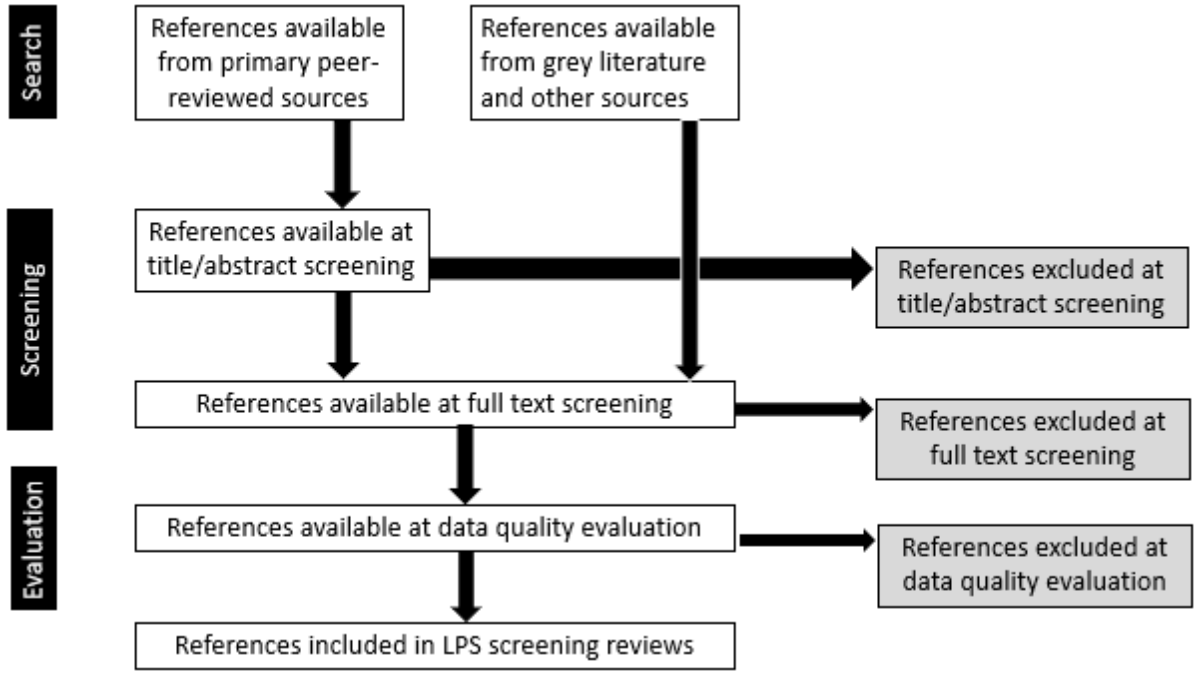
Appendix C: Literature Search Outcomes

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 3-methoxybutyl acetate. Search outcomes and reference details are provided on the candidate's HERO[62] project page.

EPA created a fit-for-purpose process to transparently document the literature search and review[63] of available hazard and fate information for low-priority substance (LPS) candidates. References from peer-reviewed primary sources, grey sources,[64] 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



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

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

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

C.1.1 Search for Analog Data

To supplement the information on the candidate chemical, 3-methoxybutyl acetate, the following analog was used for designation: 3-methoxybutanol (CASRN 2517-43-3). Acetic acid, 2-methoxypropyl ester (CASRN 70657-70-4) was also considered as an analog but not used for designation. For more details and justification on the analog, see section 6.1.1. Analogs were used to fill data gaps on endpoints for which 3-methoxybutyl acetate lacked quality data, such as skin irritation, or to add to the weight of 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 3-methoxybutyl acetate described above.[63]

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 3-methoxybutyl 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 3-methoxybutyl acetate. For grey literature and other secondary sources, Table C.3 lists the search terms used for 3-methoxybutyl acetate and analogs.

Table C.2: Search Terms Used in Peer Reviewed Databases		
Discipline	**Database**	**Search terms**[65]
Human Health	PubMed	4435-53-4[rn] OR "3-methoxybutyl acetate"[nm] OR "1-Butanol, 3-methoxy-, 1-acetate"[tw] OR "1-Butanol, 3-methoxy-, acetate"[tw] OR "3-Methoxybutyl acetate"[tw] OR "Acetic acid, 3-methoxybutyl ester"[tw] OR "Methoxybutyl acetate, 3-"[tw] OR "Methyl-1,3-butylene glycol acetate"[tw] OR "3-methoxy-1-butanol, acetate"[tw] OR ("butoxyl"[tw] NOT ("butoxyl radical"[tw] OR "butoxyl radicals"[tw] OR "tert-butoxyl radical"[tw] OR "tert-butoxyl radicals"[tw] OR "t-butoxyl radical"[tw] OR "t-butoxyl radicals"[tw]))
	Toxline	(4435-53-4 [rn] OR "1-butanol 3-methoxy- 1-acetate" OR "1-butanol 3-methoxy-acetate" OR "3-methoxybutyl acetate" OR "acetic acid 3-methoxybutyl ester" OR "methoxybutyl acetate 3-" OR "methyl-1 3-butylene glycol acetate" OR "3-methoxy-1-butanol acetate" OR ("butoxyl" NOT "butoxyl radical")) AND (ANEUPL [org] OR BIOSIS [org] OR CIS [org] OR DART [org] OR EMIC [org] OR EPIDEM [org] OR FEDRIP [org] OR HEEP [org] OR HMTC [org] OR IPA [org] OR RISKLINE [org] OR MTGABS [org] OR NIOSH [org] OR NTIS [org] OR PESTAB [org] OR PPBIB [org]) AND NOT PubMed [org] AND NOT pubdart [org]
	TSCATS 1	4435-53-4[rn] AND tscats[org]
	WOS	TS=("4435-53-4" OR "1-Butanol, 3-methoxy-, 1-acetate" OR "1-Butanol, 3-methoxy-, acetate" OR "3-Methoxybutyl acetate" OR "Acetic acid, 3-methoxybutyl ester" OR "Methoxybutyl acetate, 3-" OR "Methyl-1,3-butylene glycol acetate" OR "3-methoxy-1-butanol, acetate") OR (TS="butoxyl" NOT TS=("butoxyl radical" OR "butoxyl radicals"))
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	"4435-53-4" OR "1-Butanol, 3-methoxy-, 1-acetate" OR "1-Butanol, 3-methoxy-, acetate" OR "3-Methoxybutyl acetate" OR "Acetic acid, 3-methoxybutyl ester" OR "Methoxybutyl acetate, 3-" OR "Methyl-1,3-butylene glycol acetate" OR "3-methoxy-1-butanol, acetate" OR "butoxyl"
Fate	WOS	Same as human health strategy synonyms only

Table C.3: Search Terms Used in Grey Literature and Additional Sources	
Chemical	**Search terms**
3-Methoxybutyl Acetate	Searched as a string or individually depending on source: “4435-53-4” OR "1-Butanol, 3-methoxy-, 1-acetate" OR "1-Butanol, 3-methoxy-, acetate" OR "3-Methoxybutyl acetate" OR "Acetic acid, 3-methoxybutyl ester" OR "Butoxyl" OR "Methoxybutyl acetate, 3-" OR "Methyl-1,3-butylene glycol acetate"
Analogs searched	acetic acid, 2-methoxypropyl ester (CASRN 70657-70-4); 3-methoxybutanol (CASRN 2517-43-3)

After the search terms were applied, more than 290 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

[65] 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.

and evaluated through the LPS literature search and review process.[63] Of these, 12 references were included for data evaluation and used to support the designation of 3-methoxybutyl 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 3-methoxybutyl 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[63] 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 3-methoxybutyl acetate, EPA excluded a total of 173 references when assessing human health hazard. Off-topic references (e.g., studies that did not contain information relevant to human health) were excluded at either title/abstract screening (see Table C.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[66] relevant to human health hazard									
84538	4854457	4376428	4854502	4851240	4854543	2871084	4854477	4851219	4854522
525496	4854458	4770843	4854503	4851255	4854544	2875597	4854478	4851220	4854523
611384	4854459	4834290	4854504	4851272	4854545	2881863	4854479	4851221	4854524
611386	4854460	4851206	4854505	4851281	4854546	2910708	4854480	4851223	4854525
666559	4854461	4851207	4854506	4851287	4854548	3244746	4854481	4851224	4854526
837554	4854462	4851208	4854508	4851315	4854549	3378876	4854482	4851225	4854527
891128	4854463	4851209	4854509	4854454	4854550	3379632	4854483	4851226	4854528
1016309	4854465	4851210	4854510	4854455	4854551	3390578	4854484	4851227	4854529
1182099	4854467	4851211	4854511	4854456	4854553	3407270	4854485	4851228	4854530
1205739	4854468	4851212	4854512	4854532	4854556	3829850	4854486	4851229	4854531
1468551	4854469	4851213	4854514	4854533	4854558	3865611	4854487	4233057	4854590
1613340	4854470	4851214	4854515	4854534	4854559	4071919	4854489	4318601	4854591
2123950	4854471	4851215	4854516	4854535	4854560	4144981	4854490	4348711	4854592
2713362	4854472	4851216	4854517	4854536	4854561	4181676	4854491	4348712	4854595
2807532	4854473	4851217	4854520	4854537	4854562	4182379	4854495	4348713	4854496
2823859	4854475	4851218	4854521	4854539	4854588	4854499	4854501		
Reference excluded (HERO ID) because the reference primarily contained *in silico* data									
N/A.									

[66] 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)**
Does the reference contain information pertaining to a low-priority substance candidate?	No	2771396 4839288 4839294 4851335 4839280 4839285 4839286
What type of source is this reference?	Review article or book chapter that contains only citations to primary literature sources	N/A.
What kind of evidence does this reference primarily contain?	*In silico* studies that DO NOT contain experimental verification	N/A.
The following question apply to HUMAN evidence only		
Does the reference report an exposure route that is or is presumed to be by an inhalation, oral, or dermal route?	No	N/A.
Does the reference report both test substance exposure(s) AND related health outcome(s)?	No	N/A.
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?	No	N/A.
Note: If the paper does not pertain to mixtures, choose "Not Applicable".	No	N/A.
The following question apply to ANIMAL evidence only		
Does the reference report an exposure route that is by inhalation, oral, or dermal route?	No	4839290
Does the reference report both test substance-related exposure(s) AND related health outcome(s)?	No	4839285 4839290 4839493
Does the reference report the duration of exposure?	No	5093624
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	4839493

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 paper report a negative control that is a vehicle control or no treatment control?	No[67]	4839493 4839493 4839290 4839282 4839285 4839282 5093921
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	4839279
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	4839290
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.	5093729 5093827
Metric 2: Negative and Vehicle Controls	A concurrent negative control group was not included or reported. **OR** The reported negative control group was not appropriate (e.g., age/weight of animals differed between control and treated groups).	N/A.
Metric 3: Positive Controls	When applicable, an appropriate concurrent positive control (i.e., inducing a positive response) was not used.	5094005

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

Table C.6: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Human Health Hazard – Animal		
Data Quality Metric	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 4: Reporting of Doses/Concentrations	Doses/concentrations were not reported and could not be calculated using default or reported estimates of body weight and diet/water intake (e.g., default intake values are not available for pregnant animals).	N/A.
Metric 5: Exposure Duration	The duration of exposure was not reported. **OR** The reported exposure duration was not suited to the study type and/or outcome(s) of interest (e.g., <28 days for repeat dose).	N/A.
Metric 6: Test Animal Characteristics	The test animal species was not reported. **OR** The test animal (species, strain, sex, life-stage, source) was not appropriate for the evaluation of the specific outcome(s) of interest (e.g., genetically modified animals, strain was uniquely susceptible or resistant to one or more outcome of interest).	N/A.
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).	5093827 5094005 5093625
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.).	4839289 5093625
Metric 9: Reporting of Data	Data presentation was inadequate (e.g., the report does not differentiate among findings in multiple exposure groups). **OR**	5094005 5093625

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)**
	Major inconsistencies were present in reporting of results.	

Table C.7: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Human Health Hazard – In Vitro		
Data Quality Metric	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 1: Test Substance Identity	The test substance identity or description cannot be determined from the information provided (e.g., nomenclature was unclear and CASRN or structure were not reported). **OR** For mixtures, the components and ratios were not characterized or did not include information that could result in a reasonable approximation of components.	4839280
Metric 2: Negative Controls	A concurrent negative control group was not included or reported. **OR** The reported negative control group was not appropriate (e.g., different cell lines used for controls and test substance exposure).	N/A.
Metric 3: Positive Controls	A concurrent positive control or proficiency group was not used.	N/A.
Metric 4: Assay Type	The assay type was not reported. **OR** The assay type was not appropriate for the study type or outcome of interest (e.g., *in vitro* skin corrosion protocol used for *in vitro* skin irritation assay).	N/A.
Metric 5: Reporting of Concentration	The exposure doses/concentrations or amounts of test substance were not reported.	N/A.
Metric 6: Exposure Duration	No information on exposure duration(s) was reported. **OR** 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 7: Metabolic Activation	No information on the characterization and use of a metabolic activation system was reported.	N/A.

Table C.7: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Human Health Hazard – In Vitro		
Data Quality Metric	**Unacceptable if:**	**References excluded (HERO ID)**
	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).	
Metric 8: Test Model	The test model was not reported **OR** The test model was not routinely used for evaluation of the specific outcome of interest.	N/A.
Metric 9: Outcome Assessment Methodology	The outcome assessment methodology was not reported. **OR** The assessment methodology was not appropriate for the outcome(s) of interest (e.g., cells were evaluated for chromosomal aberrations immediately after exposure to the test substance instead of after post-exposure incubation period).	N/A.

C.2.2 Environmental Hazard

For the screening review of this LPS candidate 3-methoxybutyl acetate, EPA excluded a total of 243 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[68] relevant to environmental hazard									
84538	4851305	4851243	4854506	4348713	4854468	2875597	4851331	4851273	4854534
525496	4851307	4851244	4854508	4376428	4854469	2881863	4851332	4851275	4854535
611384	4851309	4851246	4854509	4665318	4854470	2910708	4851333	4851276	4854536
611386	4851310	4851247	4854510	4770843	4854471	3244746	4851334	4851277	4854537
666559	4851311	4851248	4854511	4834290	4854472	3378876	4851335	4851278	4854539
837152	4851312	4851249	4854512	4851206	4854473	3379632	4854450	4851280	4854540
837554	4851313	4851250	4854514	4851207	4854475	3390578	4854451	4851281	4854541

[68] 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.8: Off-Topic References Excluded at Title/Abstract Screening for Environmental Hazard									
891128	4851314	4851251	4854515	4851208	4854477	3400664	4854454	4851282	4854542
1016309	4851315	4851252	4854516	4851209	4854478	3407270	4854455	4851283	4854543
1036343	4851316	4851253	4854517	4851211	4854479	3829850	4854456	4851284	4854544
1182099	4851317	4851254	4854520	4851212	4854480	3865611	4854457	4851286	4854545
1205739	4851318	4851255	4854521	4851213	4854481	4144981	4854458	4851287	4854546
1468551	4851319	4851256	4854522	4851214	4854482	4181676	4854459	4851289	4854548
1613340	4851320	4851257	4854523	4851215	4854483	4182379	4854460	4851290	4854549
1788641	4851321	4851259	4854524	4851216	4854484	4233057	4854461	4851292	4854550
1940095	4851322	4851262	4854525	4851217	4854485	4318601	4854462	4851294	4854551
2123950	4851323	4851263	4854526	4851218	4854486	4326452	4854463	4851295	4854553
2572747	4851324	4851264	4854527	4851219	4854487	4348711	4854465	4851297	4854556
2713362	4851325	4851265	4854528	4851220	4854489	4348712	4854467	4851302	4854558
2807532	4851326	4851266	4854529	4851223	4854490	2849947	4851329	4851271	4854532
2823859	4851327	4851267	4854530	4851224	4854491	2871084	4851330	4851272	4854533
2836016	4851328	4851270	4854531	4851225	4854495	4851226	4854496	4851228	4854497
4854505	4851229	4851230	4851232	4851234	4854559	4854561	4854588	4854591	4854595
4854499	4854501	4851231	4851233	4851241	4854560	4854562	4854590	4854592	4854498
4854503	4854502	4854504							
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	N/A.
What type of source is this reference?	Review article or book chapter that contains only citations to primary literature sources	N/A.
Is quantitative environmental hazard data presented?	No	N/A.
Is this primarily a modeling/simulation study? [Note: select "No" if experimental verification was included in the study]	Yes	N/A.
Is environmental hazard data presented for standard or non-standard aquatic or terrestrial species (fish, invertebrates, microorganisms, non-mammalian terrestrial species)?	No	N/A.
Is exposure measured for the target substance or is the test substance a mixture (except for reasonable impurities, byproducts, and aqueous solutions) or formulated product?	Mixture	N/A.
	Formulated Product	N/A.
Does the reference report a duration of exposure?	No	N/A.

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 report a negative control that is a vehicle control or no treatment control?	No	4839256 4839257
Does the reference include endpoints in the information needs?	No	N/A.

Table C.10: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Environmental Hazard		
Question	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 1: Test Substance Identity	The test substance identity or description cannot be determined from the information provided (e.g., nomenclature was unclear, CASRN or structure were not reported, substance name/ description does not match CASRN). **OR** For mixtures, the components and ratios were not characterized or did not include information that could result in a reasonable approximation of components.	N/A.
Metric 2: Negative Controls	A concurrent negative control group was not included or reported.	4839257
Metric 3: Experimental System	The experimental system (e.g., static, semi-static, or flow-through regime) was not described.	N/A.
Metric 4: Reporting of Concentrations	Test concentrations were not reported.	4839257
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.	4839252 4839257
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 this LPS candidate 3-methoxybutyl acetate, EPA excluded a total of 161 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[69] relevant to environmental fate									
84538	4854468	4851207	4854516	2881863	4854489	4851229	4854536	4854588	84538
525496	4854469	4851208	4854517	2910708	4854490	4851230	4854537	4854590	525496
611384	4854470	4851209	4854520	3244746	4854491	4851231	4854539	4854591	611384
611386	4854471	4851211	4854521	3378876	4854495	4851232	4854540	4854592	611386
666559	4854472	4851212	4854522	3379632	4854496	4851233	4854541	4854595	666559
837554	4854473	4851213	4854523	3390578	4854497	4851234	4854542	4854562	837554
891128	4854475	4851214	4854524	3407270	4854498	4851272	4854543	4854467	891128
1016309	4854477	4851215	4854525	3829850	4854499	4851281	4854544	4854561	1016309
1182099	4854478	4851216	4854526	3865611	4854501	4851312	4854545	4854465	1182099
1205739	4854479	4851217	4854527	4144981	4854502	4854454	4854546	4854514	1205739
1468551	4854480	4851218	4854528	4181676	4854503	4854455	4854548	4834290	1468551
1613340	4854481	4851219	4854529	4182379	4854504	4854456	4854549	4854560	1613340
2123950	4854482	4851220	4854530	4233057	4854505	4854457	4854550	4854463	2123950
2713362	4854483	4851223	4854531	4318601	4854506	4854458	4854551	4854512	2713362
2807532	4854484	4851224	4854532	4348711	4854508	4854459	4854553	4770843	2807532
2823859	4854485	4851225	4854533	4348712	4854509	4854460	4854556	4854515	2823859
2871084	4854486	4851226	4854534	4348713	4854510	4854461	4854558	4851206	2871084
Reference excluded (HERO ID) because the reference did NOT present quantitative environmental fate data									
N/A.									

Table C.12: Screening Questions and Off-Topic References Excluded at Full Text Screening for Fate

Question	Off-topic if answer is:	References excluded (HERO ID)
Does the reference contain information pertaining to a low- priority substance candidate?	No	N/A.
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.

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

Table C.13: Data Quality Metrics and Unacceptable References Excluded at Data Quality Evaluation for Fate		
Data quality metric	**Unacceptable if:**	**References excluded (HERO ID)**
Metric 1: Test Substance Identity	The test substance identity or description cannot be determined from the information provided (e.g., nomenclature was unclear and CASRN or structure were not reported). **OR** For mixtures, the components and ratios were not characterized or did not include information that could result in a reasonable approximation of components.	N/A.
Metric 2: Study Controls	The study did not include or report crucial control groups that consequently made the study unusable (e.g., no positive control for a biodegradation study reporting 0% removal). **OR** The vehicle used in the study was likely to unduly influence the study results.	N/A.
Metric 3: Test Substance Stability	There were problems with test substance stability, homogeneity, or preparation that had an impact on concentration or dose estimates and interfered with interpretation of study results.	N/A.
Metric 4: Test Method Suitability	The test method was not reported or not suitable for the test substance. **OR** The test concentrations were not reported. **OR** 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.	4839261 4839422
Metric 5: Testing Conditions	Testing conditions were not reported, and the omission would likely have a substantial impact on study results. **OR** Testing conditions were not appropriate for the method (e.g., a biodegradation study at temperatures that inhibit the microorganisms).	N/A.
Metric 6: System Type and Design- Partitioning	Equilibrium was not established or reported, preventing meaningful interpretation of study results. **OR** The system type and design (e.g. static, semi-static, and flow-through; sealed, open) were not capable of appropriately maintaining substance concentrations, preventing meaningful interpretation of study results.	N/A.
Metric 7: Test Organism-Degradation	The test organism, species, or inoculum source were not reported, preventing meaningful interpretation of the study results.	N/A.
Metric 8: Test Organism-Partitioning	The test organism information was not reported. **OR** The test organism is not routinely used and would likely prevent meaningful interpretation of the study results.	N/A.
Metric 9: Outcome Assessment Methodology	The assessment methodology did not address or report the outcome(s) of interest.	N/A.

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 10: Data Reporting	Insufficient data were reported to evaluate the outcome of interest or to reasonably infer an outcome of interest. **OR** The analytical method used was not suitable for detection or quantification of the test substance. **OR** Data indicate that disappearance or transformation of the parent compound was likely due to some other process.	N/A.
Metric 11: Confounding Variables	There were sources of variability and uncertainty in the measurements and statistical techniques or between study groups.	4839261 4839422
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.