ETHYL LACTATE

(CAS #687-47-8)

GREENSCREEN® FOR SAFER CHEMICALS (GREENSCREEN®) ASSESSMENT

Prepared by:

ToxServices LLC

Assessment Date: February 24, 2025[1]

Expiration Date: February 24, 2030

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[1] The report was last updated on February 24, 2025. However the last complete literature search was conducted on December 19, 2024.

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GreenScreen® Executive Summary for Ethyl Lactate (CAS #687-47-8)

Ethyl lactate is the ester of lactic acid and ethanol. It is a flammable colorless liquid used as a solvent and a flavoring agent in food, as well as an anti-acne agent in cosmetic products. Ethyl lactate is a liquid under standard temperature and pressure. It has a high measured vapor pressure, indicating that it is volatile. It is miscible in water with a water solubility of 1,004 kg/L.

Ethyl lactate was assigned a **GreenScreen Benchmark™ Score of 2** ("Use but Search for Safer Substitutes"). This score is based on the following hazard score combinations:

- Benchmark 2e
  - Moderate Group I Human Toxicity (developmental toxicity-D and endocrine activity-E)
- Benchmark 2f
  - Very High Group II Human Toxicity (eye irritation-IrE)

New Approach Methodologies (NAMs) used in this GreenScreen® include *in silico* modeling for endocrine activity, respiratory sensitization, and chronic aquatic toxicity, and *in vitro* testing for genotoxicity, endocrine activity, and eye irritation. The quality, utility, and accuracy of NAM predictions are greatly influenced by two primary types of uncertainties:

- Type I: Uncertainties related to the input data used
- Type II: Uncertainties related to extrapolations made

Type I (input data) uncertainties in ethyl lactate's NAMs dataset include lack of sufficient data for endocrine activity, respiratory sensitization, eye irritation, and chronic aquatic toxicity, and lack of validated test methods for respiratory sensitization. Ethyl lactate's Type II (extrapolation output) uncertainties include the lack of a defined applicability domain of OECD Toolbox structural alerts and ToxCast models, limitations of *in vitro* genotoxicity tests in mimicking *in vivo* metabolism and their focusing on only a few events in genotoxicity, unclear *in vivo* relevance of *in vitro* receptor binding activity assays due to lack of consideration of toxicokinetics, incomplete coverage of endocrine pathways in the Tox21 EDSP program, inability of single *in vitro* skin or eye tests to determine GHS classifications, and lack of consideration of non-immunological mechanisms of respiratory sensitization.

GreenScreen® Hazard Summary for Ethyl Lactate

Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
C	M	R	D	E	AT	ST		N		SnS	SnR	IrS	IrE	AA	CA	P	B	Rx	F
						s	r*	s	r*	*	*								
L	**L**	*L*	*M*	*M*	**L**	**M**	**L**	*M*	**L**	**L**	*L*	**L**	**vH**	**L**	*L*	*vL*	**vL**	*L*	**M**

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect lower confidence in the hazard classification while hazard levels in **BOLD** font reflect higher confidence in the hazard classification. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they have four hazard scores (i.e., vH, H, M, and L) instead of three (i.e., H, M, and L), and are based on single exposures instead of repeated exposures. Group II* Human Health endpoints are indicated by an * after the name of the hazard endpoint or after "repeat" for repeated exposure sub-endpoints. Please see Appendix A for a glossary of hazard acronyms.

GreenScreen® Chemical Assessment for Ethyl Lactate (CAS #687-47-8)

Method Version: GreenScreen® Version 1.4
Assessment Type[2]: Certified
Assessor Type: Licensed GreenScreen® Profiler

GreenScreen® Assessment (v.1.4) Prepared By:
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Title: Toxicologist
Organization: ToxServices LLC
Date: November 26, 2024; February 19, 2025

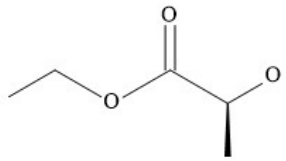
Quality Control Performed By:
Name: Bingxuan Wang, Ph.D., D.A.B.T.
Title: Senior Toxicologist
Organization: ToxServices LLC
Date: December 19, 2024; February 24, 2025

Expiration Date: February 24, 2030[3]

Chemical Name: Ethyl lactate

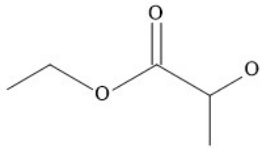
CAS Number: 687-47-8

Chemical Structure(s):



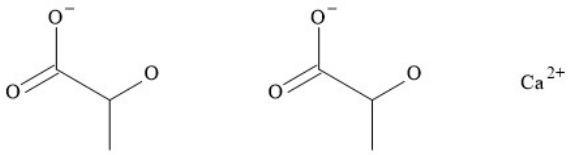
Also called:
Ethyl L-lactate; ethyl (2S)-2-hydroxypropanoate; Ethyl L-(-)-Lactate; (S)-ethyl 2-hydroxypropanoate; (L)-ethyl lactate; (L)-(-)-ethyl lactate; ethyl (2S)-lactate; Propanoic acid, 2-hydroxy-, ethyl ester, (2S)-; Ethyl (S)-2-hydroxypropionate; (S)-Ethyl lactate; L-Lactic acid ethyl ester; (S)-(+)-ethyl lactate; (S)-(-)-ethyl lactate; (2S)-2-hydroxy-propionic acid ethyl ester (PubChem 2024)

Suitable surrogates or moieties of chemicals used in this assessment (CAS #'s):
There are some data gaps for ethyl lactate. The CAS number of 647-47-8 refers to the 2S enantiomer of ethyl lactate. Therefore, the racemic mixture of the 2R and 2S enantiomers of ethyl lactate, with the CAS #97-64-3, was used to address data gaps. Due to a lack of carcinogenicity data available, calcium lactate (CAS #814-80-2) and ethanol (CAS #50-21-5) are used as surrogates, as they represent the lactate and ethanol hydrolysis products, respectively.

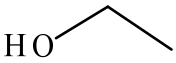


Ethyl lactate (CAS #97-64-3)

[2] GreenScreen® reports are either "UNACCREDITED" (by unaccredited person), "AUTHORIZED" (by Authorized GreenScreen® Practitioner), or "CERTIFIED" (by Licensed GreenScreen® Profiler or equivalent).
[3] Assessments expire five years from the date of completion starting from January 1, 2019. An assessment expires three years from the date of completion if completed before January 1, 2019 (CPA 2018a).



Calcium lactate (CAS #814-80-2)



Ethanol (CAS# 64-17-5)

Identify Applications/Functional Uses (PubChem 2024)**:**
1. Solvent
2. Flavoring agent
3. Anti-acne agent

Known Impurities[4]:
No information is available. The screen is performed on the theoretical pure substance.

GreenScreen® Summary Rating for Ethyl Lactate[5,6 7,8]: Ethyl lactate was assigned a **GreenScreen Benchmark™ Score of 2** ("Use but Search for Safer Substitutes") (CPA 2018b). This score is based on the following hazard score combinations:

- Benchmark 2e
  - Moderate Group I Human Toxicity (developmental toxicity-D and endocrine activity-E)
- Benchmark 2f
  - Very High Group II Human Toxicity (eye irritation-IrE)

Figure 1: GreenScreen® Hazard Summary for Ethyl Lactate

Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
C	M	R	D	E	AT	ST		N		SnS	SnR	IrS	IrE	AA	CA	P	B	Rx	F
						s	r*	s	r*	*	*								
L	**L**	*L*	*M*	*M*	**L**	**M**	**L**	*M*	**L**	**L**	*L*	**L**	**vH**	**L**	*L*	*vL*	**vL**	*L*	**M**

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect lower confidence in the hazard classification while hazard levels in **BOLD** font reflect higher confidence in the hazard classification. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they have four hazard scores (i.e., vH, H, M, and L) instead of three (i.e., H, M, and L), and are based on single exposures instead of repeated exposures. Group II* Human Health endpoints are indicated by an * after the name of the hazard endpoint or after "repeat" for repeated exposure sub-endpoints. Please see Appendix A for a glossary of hazard acronyms.

[4] Impurities of the chemical will be assessed at the product level instead of in this GreenScreen®.
[5] For inorganic chemicals with low human and ecotoxicity across all hazard endpoints and low bioaccumulation potential, persistence alone will not be deemed problematic. Inorganic chemicals that are only persistent will be evaluated under the criteria for Benchmark 4.
[6] See Appendix A for a glossary of hazard endpoint acronyms.
[7] For inorganic chemicals only, see GreenScreen® Guidance v1.4 Section 12 (Inorganic Chemical Assessment Procedure).
[8] For Systemic Toxicity and Neurotoxicity, repeated exposure data are preferred. Lack of single exposure data is not a Data Gap when repeated exposure data are available. In that case, lack of single exposure data may be represented as NA instead of DG. See GreenScreen® Guidance v1.4 Annex 2.

Environmental Transformation Products

Per GreenScreen® guidance (CPA 2018b), chemicals that degrade rapidly and completely (i.e., meet criteria for a Very Low for persistence) are not likely to form persistent biodegradation intermediates because the degradation intermediates will not persist long enough to be encountered after use or release of the parent chemical (i.e., relevant). As ethyl lactate is readily biodegradable, it is not expected to have relevant transformation products.

Introduction

Ethyl lactate is the ester of lactic acid and ethanol. It is a flammable colorless liquid used as a solvent and a flavoring agent in food, as well as an anti-acne agent in cosmetic products (PubChem 2024).

ToxServices assessed ethyl lactate against GreenScreen® Version 1.4 (CPA 2018b) following procedures outlined in ToxServices' SOPs (GreenScreen® Hazard Assessment) (ToxServices 2021).

U.S. EPA Safer Choice Program's Safer Chemical Ingredients List

The SCIL is a list of chemicals that meet the Safer Choice standard (U.S. EPA 2024a). It can be accessed at: http://www2.epa.gov/saferchoice/safer-ingredients. Chemicals on the SCIL have been assessed for compliance with the Safer Choice Standard and Criteria for Safer Chemical Ingredients (U.S. EPA 2024b).

Ethyl lactate is listed on the U.S. EPA SCIL is a gray square (may not be acceptable for use in products that are candidates for the Safer Choice label and any currently certified products that contain it) with a note that it will no longer be listed on the SCIL starting 9/30/2025, and is not used in Safer Choice-certified products (U.S. EPA 2024b).

GreenScreen® List Translator Screening Results

The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to identify GreenScreen Benchmark™ 1 chemicals (CPA 2018b). Pharos (Pharos 2024) is an online list-searching tool that is used to screen chemicals against all of the lists in the List Translator electronically. ToxServices also checks the U.S. Department of Transportation (U.S. DOT) lists (U.S. DOT 2008a,b),[9] which are not considered GreenScreen® Specified Lists but are additional information sources, in conjunction with the Pharos query. The output indicates benchmark or possible benchmark scores for each human health and environmental endpoint. The output for ethyl lactate can be found in Appendix C.

- Ethyl lactate is an LT-UNK chemical when screened using Pharos, and therefore a full GreenScreen® is required.
- Ethyl lactate is listed on the U.S. DOT list as a Hazard Class 3 chemical, Packing Group III (U.S. DOT 2008a,b).
- Ethyl lactate is on the following list for multiple endpoints:
    - German FEA – Substances Hazardous to Waters: Class 1 – Low Hazard to Waters
- Specified lists for single endpoints are reported in individual hazard endpoints in the hazard assessment section below.

[9] DOT lists are not required lists for GreenScreen® List Translator v1.4. They are reference lists only.

Hazard Statement and Occupational Control

Globally Harmonized System of Classification and Labelling of Chemicals (GHS) hazard statements that are harmonized across the European Union (EU identified for ethyl lactate are indicated in Table 1, below. General personal protective equipment (PPE) recommendations are presented in Table 2, below. No occupational exposure limits (OELs) were identified.

Table 1: GHS H Statements for Ethyl Lactate (CAS #687-47-8) (ECHA C&L, CAS #687-47-8, 2024)

H Statement	H Statement Details
H226	Flammable liquid and vapor
H318	Causes serious eye damage
H335	May cause respiratory irritation

Table 2: Occupational Exposure Limits and Recommended Personal Protective Equipment for Ethyl Lactate (CAS #687-47-8)

Personal Protective Equipment (PPE)	Reference	Occupational Exposure Limits (OEL)	Reference
Eye/face: face shield and safety glasses conforming to EN 166 Hand: Butyl rubber gloves Body: Long-sleeved protective clothing Respiratory: Half-face mask (DIN EN 140) in case of insufficient ventilation	ECHA, CAS #687-47-8, 2024	N/A	N/A

Physicochemical Properties of Ethyl Lactate

Ethyl lactate is a liquid under standard temperature and pressure. It has a high measured vapor pressure, indicating that it may form a vapor. It is miscible in water with a water solubility of 1,004 kg/L (based on 8.5 mol solubilized in 1L of water). The measured log K_{ow} of 0.7 for the enantiomeric form indicates that it is not likely to bioaccumulate in aquatic biota.

Table 3: Physical and Chemical Properties of Ethyl Lactate (CAS #687-47-8)

Property	Value	Reference
Molecular formula	$C_5H_{10}O_3$	PubChem 2024
SMILES Notation	CCOC(=O)[C@H](C)O	PubChem 2024
Molecular weight	118.13 g/mol	PubChem 2024
Physical state	Liquid	PubChem 2024
Appearance	Clear and colorless	PubChem 2024
Melting point	-9°C (OECD Guideline 102)	ECHA, CAS #687-47-8, 2024
Boiling point	154°C (OECD Guideline 103)	ECHA, CAS #687-47-8, 2024
Vapor pressure	3.9 mm Hg at 20°C (OECD Guideline 104)	ECHA, CAS #687-47-8, 2024
Water solubility	1,004 kg/L at 20°C (miscible) (exp.)	ECHA, CAS #687-47-8, 2024

Table 3: Physical and Chemical Properties of Ethyl Lactate (CAS #687-47-8)		
Property	**Value**	**Reference**
Dissociation constant	pKa = 11.6 at 25°C (est.)	ECHA, CAS #687-47-8, 2024
Density/specific gravity	1.0348 g/cm^3 at 20°C (exp.)	ECHA, CAS #687-47-8, 2024
Partition coefficient	Log K_{ow} = 0.7 at 25°C (OECD Guideline 117) (surrogate racemic mixture)	ECHA, CAS #97-64-3, 2024

Toxicokinetics

Ethyl lactate is readily absorbed by the oral, dermal, and inhalation routes of exposure. Simple esters such as ethyl lactate readily undergo enzymatic hydrolysis into its component acid and alcohol components ethyl alcohol and lactic acid, both of which are common food constituents. The metabolic fate of ethyl alcohol is well known, while lactic acid is a normal and essential intermediate in human metabolism (JECFA 1982).

Hazard Classification Summary

Group I Human Health Effects (Group I Human)

Carcinogenicity (C) Score (H, M, or L): L

Ethyl lactate was assigned a score of Low for carcinogenicity based on measured data for surrogates calcium lactate and ethanol (non-alcoholic drink applications). GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is high as it is based on reliable experimental data from strong surrogates.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #50-21-5, 2024
  - *Oral: Surrogate: Calcium lactate (CAS #50-21-5):* In a 2-year carcinogenicity study (GLP status unknown) conducted in a similar manner to OECD Guideline 453, F344 rats (50/dose/sex) received calcium lactate (purity > 97%) in drinking water *ad libitum* at concentrations of 0, 2.5 or 5%. Clinical signs, mortality, body weight, water consumption, hematology, clinical chemistry, organ weights, gross pathology and histopathology were evaluated. No statistically significant dose-related increase of tumor incidences was found in any organ or tissue. The results indicated that calcium lactate was not carcinogenic in the study and the authors of the REACH dossier assigned a NOAEL of 5% (Klimisch 2, reliable with restrictions).
- ECHA, CAS #50-21-5, 2024
  - *Oral: Surrogate: Ethanol (CAS# 50-21-5):* In a GLP-compliant carcinogenicity study conducted according to Guideline EPA OPPTS 870.4200, B6C3F1 mice (48/sex/dose) received ethanol (purity 92.6%) in drinking water *ad libitum* daily at concentrations of 0, 2.5, or 5% for 2 years (105 weeks). The equivalent time-weighted average doses were 0, 2,600, and 4,250 mg/kg/day for males and 0, 2,050, and 4,400 mg/kg/day for females, respectively, according to the authors of the REACH dossier. Clinical signs, mortality, body weight, food and water consumption, organ weights, gross pathology and histopathology

were evaluated. A dose-dependent increase in the incidence of hepatocellular adenoma and carcinoma combined was reported in males with a significant increase in the incidence of hepatocellular carcinoma in the high dose male treatment group. An increase in alveolar and bronchiolar carcinoma was also observed in a dose-dependent manner in males; this included multiple and alveolar and bronchiolar carcinoma combined. No effects were reported in females. The authors of the REACH dossier stated that while there appears to be an increase in the rate of hepatic adenomas and adenoma/carcinomas combined and in lung adenomas and carcinomas compared to controls, it is apparent that these are common spontaneous tumors and the rates fall within the range of historic controls. The authors of the REACH dossier were unable to conclude whether or not ethanol caused cancer in mice in this study. Klimisch 2, reliable with restrictions).

    - *Oral: Surrogate: Ethanol (CAS# 50-21-5):* In a carcinogenicity study (GLP status unknown) conducted in a manner similar to OECD Guideline 451, Sprague Dawley rats (50/sex/dose) received ethanol via feed for 2 years (104 weeks) at concentrations of 0, 1, or 3% (equivalent to 1,000 and 3,000 mg/kg/day according to the authors of the REACH dossier). Clinical signs, mortality, body weight, organ weights, gross pathology and histopathology were evaluated. No significant increase in tumor incidence was reported in any of the treated animals. However, in low dose females, fibroma, fibroadenoma, and adenoma of the mammary gland were statistically significantly increased, and pancreatic islet cell tumors were reduced. In high dose females, the incidence of hypophysis neoplasia was increased, and the incidence of the adrenal cortex adenomas was reduced. The authors of the REACH dossier stated that, overall, the incidence of tumors in high dose females was significantly reduced, and no dose response was detected. Based on the results of this study, the authors of the REACH dossier concluded that the test substance was not carcinogenic (Klimisch 2, reliable with restrictions).
- IARC 2012, OEHHA 2023
    - *Oral: Surrogate: Ethanol (CAS# 50-21-5):* The International Agency for Research on Cancer (IARC) and Office of Environmental Health Hazard Assessment (OEHHA) Proposition 65 classifications of ethanol as "Group 1 - Agent is Carcinogenic to humans" and "Carcinogen", respectively, are based on chronic consumption of alcoholic beverages.
- MAK Commission 2018
    - *Surrogate: Ethanol (CAS# 50-21-5):* The MAK classification of "Carcinogen Group 5 - Genotoxic carcinogen with very slight risk under MAK/BAT levels" is intended to provide protections to workers in occupational settings by establishing maximum workplace concentrations.
- In summary, surrogate calcium lactate was not carcinogenic in a 2-year carcinogenicity study in rats. Although surrogate ethanol is classified as a carcinogen by multiple agencies, this is mainly based on chronic high dose consumption of alcoholic beverages. This level of voluntary exposure would not be achieved through other routes, including from hydrolysis of ethyl lactate. Based on measured data for calcium lactate and ethanol, a score of Low was assigned.

Mutagenicity/Genotoxicity (M) Score (H, M, or L): L

Ethyl lactate was assigned a score of Low for mutagenicity/genotoxicity based on negative results for mutagenicity and clastogenicity in bacteria and/or mammalian cells *in vitro* with both ethyl lactate and its enantiomeric form. GreenScreen® criteria classify chemicals as a Low hazard for mutagenicity/genotoxicity when negative data are available for both gene mutations and chromosome aberrations, and they are not GHS classified (CPA 2018b). The confidence in the score is high as it is based on reliable experimental data for ethyl lactate and its enantiomeric form.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #687-47-8, 2024
  - *In vitro*: Ethyl lactate was negative for mutagenicity in a GLP-compliant mammalian cell mutation assay conducted according to OECD Guideline 476 with mouse lymphoma L5178Y cells exposed to ethyl lactate (99.83% purity) in RPMI 1640 medium at 0.3-1,180 µg/mL with and without metabolic activation (phenobarbital and β-naphthoflavone induced rat liver S9 mix). Positive and negative controls were used; controls used were methylmethanesulfonate and cyclophosphamide. No increases in mutations at the thymidine kinase locus were seen in the presence and absence of metabolic activation. Positive and negative controls were valid (Klimisch 1, reliable without restrictions).
  - *In vitro:* Ethyl lactate was negative for genotoxicity in a GLP-compliant *in vitro* chromosomal aberration assay conducted according to OECD Guideline 473 with human peripheral lymphocytes exposed to ethyl lactate (99.83% purity) in RPMI 1640 medium at 10-1,180 µg/mL with and without metabolic activation (S9 rat liver microsomal enzymes prepared from adult male Wistar rats). Positive and negative controls were used; controls were mitomycin C and cyclophosphamide. No increases in chromosomal aberrations were seen in the presence and absence of metabolic activation. Positive and negative controls were valid (Klimisch 1, reliable without restrictions).
  - *In vitro: Surrogate: Ethyl lactate (CAS #97-64-3):* Ethyl lactate was not mutagenic in a GLP-compliant bacterial reverse mutation assay conducted according to OECD Guideline 471 in which *Salmonella typhimurium* test strains TA98, TA100, TA1535, TA1537 and TA1538 were exposed to ethyl lactate (purity not specified) at 667-10,000 µg/plate with and without metabolic activation (Aroclor 1254 induced male SD rat liver). Positive and negative controls were used; positive controls used were 2-aminoanthracene, 2-nitrofluorene, sodium azide, and ICR-191. No increase in the mutation frequency was measured with treatment in the presence or absence of metabolic activation. Positive controls, and vehicle controls were reported as valid (Klimisch 1, reliable without restrictions).

Reproductive Toxicity (R) Score (H, M, or L): *L*

Ethyl lactate was assigned a score of Low for reproductive toxicity based on a 2-generation toxicity study with the racemic mixture of ethyl lactate. GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is low as it is based on a screening study with limited reported details.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #97-64-3, 2024
  - *Oral: Surrogate: Ethyl lactate (CAS #97-64-3):* In a GLP-compliant combined repeated dose toxicity and reproductive / developmental screening study conducted according to OECD Guideline 422, male and female Wistar rats (13 females and 10 males/dose group) were administered by gavage doses of 0, 100, 200, 500, or 800 mg/kg/day ethyl lactate (purity not specified) for 14 days prior to mating. Systemic toxicity was observed at 800 mg/kg/day with three animals dying and subsequently, the dose levels were changed to 75, 300, and 600 mg/kg/day. Dosing continued for 4 days prior to mating and through mating (14 days).

Treatment of males ended and dosing for females continued through gestation (~22 days) and for 13 days of lactation. No treatment related adverse effects were found on clinical signs, mortality, body weight, food consumption, hematology, clinical biochemistry, urinalysis, organ weights, and histopathology of the parental animals at doses other than 800 mg/kg/day. There were no effects found on reproductive function or performance, gestation length, parturition, or reproductive organ examinations. Pre-implantation and early post-implantation loss was reported at the low and mid dose groups with 4 females not becoming pregnant and 2 not littering at the low dose and 2 females not becoming pregnant and 2 not littering at the mid dose. Information on the high dose and additional reproductive parameters such as estrus cyclicity, corpora lutea, number of implantations, pregnancy index, and fertility index were not specified. Study authors identified a LOAEL of 75 mg/kg/day (the lowest dose tested) for reproductive toxicity (inclusive of developmental effects) (Klimisch 1, reliable without restriction).

- *The ECHA record for this study was confusing and limited. While study authors reported 2 females at 75 and 300 mg/kg/day each were not pregnant, and 2 pregnant dams at each of these doses did not litter, likely due to pre-implantation and early post-implantation loss, study authors concluded that there were no effects on reproductive function or performance, gestation length, parturition, or reproductive organ examinations. Further, the study authors did not distinguish reproductive and developmental effects, and identified a combined LOAEL of 75 mg/kg/day for reproductive and developmental toxicities. ToxServices therefore evaluated pre- and post-implantation loss under the developmental toxicity endpoint, and assigned a NOAEL of 600 mg/kg/day for reproductive toxicity, based on the absence of effects on reproductive function or performance, gestation length, parturition, or reproductive organ examinations as reported by the study authors.*

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M, or L): *M*
Ethyl lactate was assigned a score of Moderate for developmental toxicity based on effects in the F1 generation of rats with the racemic mixture of ethyl lactate, which corresponds to a classification of GHS Category 2. GreenScreen® criteria classify chemicals as a Moderate hazard for developmental toxicity when classified as GHS Category 2 (CPA 2018b). The confidence in the score is low based on limited study details available as well as a lack of dose response in most of the effects seen.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #97-64-3, 2024
  - *Oral: Surrogate: Ethyl lactate (CAS #97-64-3):* In the previously described GLP-compliant combined repeated dose toxicity and reproductive / developmental screening study conducted according to OECD Guideline 422, male and female Wistar rats (13 females and 10 males/dose group) were administered by gavage doses of 0, 100, 200, 500, or 800 mg/kg/day ethyl lactate (purity not specified) for 10 days prior to mating. Systemic toxicity was observed at 800 mg/kg/day with three animals dying and subsequently, the dose levels were changed to 75, 300, and 600 mg/kg/day. Dosing continued for 4 days prior to mating and through mating (14 days). Treatment of males ended and dosing for females continued through gestation (~22 days) and for 13 days of lactation. No treatment related adverse effects were found on clinical signs, mortality, body weight, food consumption, hematology, clinical biochemistry, urinalysis, organ weights, and histopathology of the parental animals at doses other than 800 mg/kg/day. Pre-implantation and early post-implantation loss was

reported at the low and mid dose groups with 4 females not becoming pregnant and 2 not littering at the low dose and 2 females not becoming pregnant and 2 not littering at the mid dose. A significant decrease in anogenital index was measured in the low and mid dose groups of male pups and at all doses in female pups. Post-natal loss was increased between PND 0 to 4 at the mid dose with clinical observations of morbidity (unspecified) in the pups. The authors of the REACH dossier assigned a LOAEL of 75 mg/kg/day for the F1 generation (Klimisch 1, reliable without restriction).

- *Ethyl lactate is classified as GHS Category 2 based on pre- and post-implantation loss, and decreased anogenital index in pups of both sexes observed in this study, in the absence of parental systemic toxicity. ToxServices did not assign GHS Category 1 as almost all of the developmental effects reported lacked dose response.*

- *Dermal: Surrogate: Ethyl lactate (CAS #97-64-3):* In a GLP-compliant developmental toxicity study conducted according to EPA OTS 798.4900, pregnant female Crl:CD®(SD)BR rats (25/dose) were administered dermal applications of 0, 517, 1,551, or 3,619 mg/kg/day ethyl lactate (purity 100%) on gestation days (GD) 6-15. No developmental effects were reported and the authors of the REACH dossier assigned a developmental NOAEL of 3,619 mg/kg/day (Klimisch 1, reliable without restriction).

Endocrine Activity (E) Score (H, M, or L): *M*

Ethyl lactate was assigned a score of Moderate for endocrine activity based on dose-dependent effects on anogenital indices in male offspring and changes in T4 levels seen in rats in a combined repeated dose toxicity and reproductive developmental screening study with the racemic mixture of ethyl lactate. GreenScreen® criteria classify chemicals as a Moderate hazard for endocrine activity when there is evidence of endocrine activity but no associated effects that warrant High scores for carcinogenicity, reproductive toxicity, developmental toxicity, and repeated dose systemic toxicity (CPA 2018b). The confidence in the score is low due to lack of other effects (such as nipple retention in male offspring) supporting anti-androgenic activity, and the occurrence of the same effects in females.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- U.S. EPA 2024c
  - Ethyl lactate was inactive in 4 out of 4 assays of estrogen agonism and antagonism, inactive for androgen receptor agonism or antagonism in 3 out of 3 assays, and inactive for thyroid receptor activity in 6 out of 6 assays of the Tox 21 high throughput *in vitro* assays performed as part of the U.S. EPA's Endocrine Disruptor Screening Program in the 21st Century (EDSP) (Appendix D).
  - Ethyl lactate was predicted to be inactive for estrogen agonism, antagonism and binding by ToxCast model CERAPP Potency Level (From Literature) (Appendix D).
- ECHA, CAS #97-64-3, 2024
  - *Oral: Surrogate: Ethyl lactate (CAS #97-64-3):* In a GLP-compliant combined repeated dose toxicity and reproductive / developmental screening study conducted according to OECD Guideline 422, male and female Wistar rats (13 females and 10 males/dose group) were administered by gavage doses of 0, 100, 200, 500, or 800 mg/kg/day ethyl lactate (purity not specified) for 10 days prior to mating. Systemic toxicity was observed at 800 mg/kg/day with three animals dying and subsequently, the dose levels were changed to 75, 300, and 600 mg/kg/day. Dosing continued for 4 days prior to mating and through mating (14 days). Treatment of males ended and dosing for females continued through gestation (~22 days) and for 13 days of lactation. A significant decrease in anogenital index was measured in the

low and mid dose groups of male pups and at all dose treatment groups in female pups. The changes in anogenital index were dose-dependent in males and females, and could not be explained by any changes in animal size at birth. T4 levels were significantly reduced in male and female pups, but the dose level(s) at which this occurred was not specified. There was no significant effect on relative thyroid weight and histological examination revealed no significant morphological changes. It is unclear whether thyroids from pups were microscopically examined (Klimisch 1, reliable without restriction).

- Based on a weight of evidence, a score of Moderate was assigned. A combined repeated dose toxicity and reproductive / developmental screening study reported a significant decrease in T4 levels in offspring of rats exposed to the racemic mixture of ethyl lactate at unspecified dose levels. In addition, there was a dose dependent decrease in anogenital indices in male offspring at the low and mid doses and in female offspring at all dose levels, which could not be explained by changes in body sizes at birth. Reduced anogenital distance in males may indicate anti-androgenic activity. However, these changes were also measured in female offspring, making their toxicological significance unclear. Further, *In vitro* Tox21 high throughput screening assays did not find ethyl lactate to exert any estrogen, androgen, or thyroid effects.

Group II and II* Human Health Effects (Group II and II* Human)

Note: Group II and Group II* endpoints are distinguished in the v 1.4 Benchmark system (the asterisk indicates repeated exposure). For Systemic Toxicity and Neurotoxicity, Group II and II* are considered sub-endpoints. See GreenScreen® Guidance v1.4, Annex 2 for more details.

Acute Mammalian Toxicity (AT) (Group II) Score (vH, H, M, or L): L

Ethyl lactate was assigned a score of Low for acute toxicity based on an oral LD_{50} > 2,000 mg/kg in rats and a 4-hour inhalation LC_{50} of > 5.4 mg/L (aerosol) for the racemic mixture of ethyl lactate. GreenScreen® criteria classify chemicals as a Low hazard for acute toxicity when oral and LD_{50} values are > 2,000 mg/kg and 4-hour inhalation LC_{50} values are > 5 mg/L (aerosol) (CPA 2018b). The confidence in the score is high as it is based on reliable experimental data on the target chemical and a strong surrogate.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #687-47-8, 2024
  - *Oral:* LD_{50} > 2,000 mg/kg in male and female Wistar rats (GLP-compliant, OECD Guideline 401) (Klimisch 1, reliable without restrictions)
  - *Inhalation: Surrogate: Ethyl lactate (CAS #97-64-3):* LC_{50} > 5.4 mg/L aerosol (4-hr) in male and female Wistar-derived rats (GLP-compliant, OECD Guideline 403) (Klimisch 1, reliable without restrictions)

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST-single) (Group II) Score (vH, H, M, or L): M

Ethyl lactate was assigned a score of Moderate for systemic toxicity (single dose) based on being classified as GHS Category 3 for transient respiratory irritation observed in rats for the racemic mixture as well as being associated with hazard statement H335 on both an authoritative and screening list. GreenScreen® criteria classify chemicals as a Moderate hazard for systemic toxicity (single dose) when they are classified as GHS Category 3 and associated with hazard statement H335 (CPA 2018b). The confidence in the score is high as it is based on reliable experimental data for a strong surrogate as well as an authoritative A list.

- Authoritative and Screening Lists
  - *Authoritative:*
    - EU GHS – H335 – May cause respiratory irritation (Specific target organ toxicity – single exposure; Respiratory tract irritation – Category 3)
  - *Screening:*
    - Australia GHS – H335 – May cause respiratory irritation (Specific target organ toxicity – single exposure; Respiratory tract irritation – Category 3)
- ECHA, CAS #687-47-8, 2024
  - *Oral*: In a GLP-compliant acute oral toxicity study conducted according to OECD Guideline 401, male and female Wistar rats (5/sex) were administered doses of 2,000 mg/kg via gavage. Animals were observed for 14 days. No mortality occurred before the scheduled sacrifice. At 1, 4, and 24 hours after treatment, all animals showed moderate signs of piloerection; there were no effects seen after 48 hours. Body weights were recorded on day 0, 3 7 and 14 of the study but the results were not reported. There were no macroscopic changes seen during necropsy (Klimisch 1, reliable without restrictions).
  - *Inhalation: Surrogate: Ethyl lactate (CAS #97-64-3):* In a GLP-compliant acute inhalation study conducted according to OECD Guideline 403, male and female Wistar-derived rats (5/sex) were exposed to concentrations of 5.4 mg/L ethyl lactate (whole body aerosol) for four hours and observed for 15 days. A decrease in breathing was seen during the exposure periods and was accompanied by wet noses after 30 minutes and piloerection after 60 minutes. Additionally, half-closed eyes and lachrymation were seen at 15 minutes after exposure; all effects were gone the following day. These effects were attributed to the irritation effects of the test substance. None of the animals died during the or after exposure. No change in body weight was measured. Upon necropsy, pale lungs were seen in one male and three females; furthermore, three females showed some petechiae. The study authors established an LC_{50} > 5.4 mg/L (Klimisch 1, reliable without restrictions).
    - *As there were some transient irritative effects seen, ethyl lactate can be classified to GHS Category 3 (UN 2023).*

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST-repeat) (Group II*) Score (H, M, or L): L

Ethyl lactate was assigned a score of Low for systemic toxicity (repeated dose) based on an oral NOAEL of 600 mg/kg/day in an oral combined repeated dose toxicity and reproductive / developmental toxicity screening study in rats with the racemic mixture of ethyl lactate. This does not warrant GHS classification. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (repeated dose) when adequate data are available and they are not classified under GHS (CPA 2018b). The confidence in the score is high as it is based on reliable data for a strong surrogate.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #97-64-3, 2024
  - *Oral: Surrogate: Ethyl lactate (CAS #97-64-3):* In a GLP-compliant combined repeated dose toxicity and reproductive / developmental toxicity screening study conducted according to OECD Guideline 422, male and female Wistar rats (13 females and 10 males/dose group) were administered by gavage doses of 0, 100, 200, 500, or 800 mg/kg/day ethyl lactate (purity not specified) for 10 days prior to mating. Systemic toxicity was observed at 800 mg/kg/day with three animals dying and subsequently, the dose levels were changed to 75, 300, and 600 mg/kg/day. Dosing continued for 4 days prior to mating and through mating

(14 days). Treatment of males ended and dosing for females continued through gestation (~22 days) and for 13 days of lactation. There was no significant effect on body weight, food consumption, hematological parameters, or urinalysis. A significant change in the relative weights of Cowper's gland, kidney, spleen, levator ani and bulbocavernosus muscles were measured, but histological examination revealed no findings in the tissues. The authors of the REACH dossier therefore did not consider body weight effects toxicologically significant and assigned a NOAEL of 600 mg/kg/day (Klimisch 1, reliable without restriction).

- *The NOAEL of 600 mg/kg/day is greater than the duration-adjusted GHS guidance value of 300 mg/kg/day for a 28-day study (i.e., 100 mg/kg/day * 3 months/1 month = 300 mg/kg/day). Therefore, ethyl lactate is not classified under GHS.*

- ECHA, CAS #687-47-8, 2024
  - *Inhalation:* In a GLP-compliant subacute inhalation toxicity study performed according to OECD Guideline 412, Wistar rats (5/sex/dose) were exposed to ethyl lactate vapors (purity 99.8%) by whole body exposure at 0, 150, 600 or 2,500 mg/m^3 (nominal) (corresponding to measured concentrations of 0, 145, 603 and 2,451 mg/m^3) 5 days per week for 4 weeks. There were histopathological changes on the nasal cavity epithelium, and the authors identified a local effects LOAEC of 150 mg/m^3. Therefore, study authors assigned a systemic toxicity NOAEC of 2,500 mg/m^3, the highest concentration tested, based on lack of treatment related systemic effects (Klimisch 1, reliable without restriction).
    - *The systemic NOAEC of 2,500 mg/m^3, equivalent to 2,500 mg/m^3 * 10^{-3} m^3/L * 5 days/7 days = 1.8 mg/L. This is lower than the duration adjusted (i.e., tripled) GHS Category 2 guidance value of 3 mg/L for vapors. Therefore, there is insufficient data for GHS classification for this study.*
  - *Inhalation:* In a GLP-compliant subacute inhalation toxicity study performed according to OECD Guideline 412, Wistar rats (5/sex/dose) were exposed to ethyl lactate vapors (purity 99.7%) by whole body exposure at 0, 25, 75 or 200 mg/m^3 (nominal) 5 days per week for 4 weeks. Additional animals (5/sex/group) from the high and control groups were included for a 28-day recovery period before sacrifice. There were no treatment related effects on survival, clinical signs, body weight, gross pathology, or histopathology. Therefore, study authors assigned a NOAEC of 200 mg/m^3, the highest concentration tested (Klimisch 1, reliable without restriction).

Neurotoxicity (single dose, N-single) (Group II) Score (vH, H, M, or L): *M*

Ethyl lactate was assigned a score of Moderate for neurotoxicity (single dose) based on qualitative description that it (or its racemic mixture) is a central nervous system depressant and associated with acute solvent syndrome, which corresponds to GHS Category 3. Although the human evidence was limited and qualitative, they were consistent across two data sources. Therefore, ToxServices conservatively relied on this information to score this endpoint. GreenScreen® criteria classify chemicals as a Moderate hazard for neurotoxicity (single dose) when classified as GHS Category 3 (CPA 2018b). The confidence in the score is low as no signs of narcotic effects were observed in an acute oral toxicity study with the target chemical in rats.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:*
    - New Zealand GHS – Specific target organ toxicity – single exposure category 3 narcotic effects
- ECHA, CAS #687-47-8, 2024

  - *Oral*: In a GLP-compliant acute oral toxicity study conducted according to OECD Guideline 401, male and female Wistar rats (5/sex) were administered doses of 2,000 mg/kg via gavage. Animals were observed for 14 days. At 1, 4, and 24 hours after treatment, all animals showed moderate signs of piloerection; there were no effects seen after 48 hours (Klimisch 1, reliable without restrictions).
- Haz-Map 2024
  - Ethyl lactate is associated with acute solvent syndrome (i.e., symptoms associated with acute exposure to organic solvents, ranging from headache, dizziness, light-headedness, unconscious, seizures, to potentially death (Dick 2006)), and chronic solvent encephalopathy.
- HSDB 2017
  - *Surrogate: Ethyl lactate (CAS #97-64-3):* Ethyl lactate is a central nervous system depressant.

Neurotoxicity (repeated dose, N-repeated) (Group II*) Score (H, M, or L): L
Ethyl lactate was assigned a score of Low for neurotoxicity (repeated dose) based on the racemic mixture not classified as a neurotoxicant under GHS. GreenScreen® criteria classify chemicals as a Low hazard for neurotoxicity (repeated dose) when adequate negative data are available and the chemical is GHS not classified (CPA 2018b). The confidence in the score is high as it is based on reliable experimental data for a strong surrogate.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #97-64-3, 2024
  - *Oral: Surrogate: Ethyl lactate (CAS #97-64-3):* In a GLP-compliant combined repeated dose toxicity and reproductive / developmental toxicity screening study conducted according to OECD Guideline 422, male and female Wistar rats (13 females and 10 males/dose group) were administered by gavage doses of 0, 100, 200, 500, or 800 mg/kg/day ethyl lactate (purity not specified) for 10 days prior to mating. Systemic toxicity was observed at 800 mg/kg/day with three animals dying and subsequently, the dose levels were changed to 75, 300, and 600 mg/kg/day. Dosing continued for 4 days prior to mating and through mating (14 days). Treatment of males ended and dosing for females continued through gestation (~22 days) and for 13 days of lactation. No effects were identified in functional battery observation tests (tail flick test and grip strength test) performed on the animals following the dosing period (Klimisch 1, reliable without restriction).
    - *ToxServices identified a neurotoxicity NOAEL of 600 mg/kg/day for this study, which was the highest dose tested. The NOAEL of 600 mg/kg/day is greater than the duration-adjusted GHS guidance value of 300 mg/kg/day for a 28-day study (i.e., 100 mg/kg/day * 3 months/1 month = 300 mg/kg/day). Therefore, ethyl lactate is not classified under GHS for neurotoxicity.*

Skin Sensitization (SnS) (Group II*) Score (H, M, or L): L
Ethyl lactate was assigned a score of Low for skin sensitization based on a lack of sensitization reactions seen in mice in a local lymph node assay (LLNA). GreenScreen® criteria classify chemicals as a Low hazard for skin sensitization when adequate negative data are available and the chemical is GHS not classified (CPA 2018b). The confidence in the score is high as it is based on reliable experimental data.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.

- ECHA, CAS #687-47-8, 2024
    - A GLP-compliant mouse LLNA was conducted according to OECD Guideline 429/EU Method B.42/EPA OPPTS 870.2600. Female CBA:J mice (5/dose) were administered doses 0, 25, 50, and 100% ethyl lactate in acetone/olive oil (4:1 v/v) on the dorsal surface of both ears for 3 consecutive days. Three days after the final application, the animals were sacrificed and lymph nodes isolated to perform the proliferation assay. The stimulation indices (SIs) for the three treated groups were 0.9, 1, and 0.8. As none of the SIs were ≥ 3, an EC_3 value could not be calculated. Therefore, the study authors concluded that ethyl lactate was not a dermal sensitizer (Klimisch 1, reliable without restrictions).

Respiratory Sensitization (SnR) (Group II*) Score (H, M, or L): *L*
Ethyl lactate was assigned a score of Low for respiratory sensitization based on the lack of dermal sensitization potential according to the ECHA guidance (2017). GreenScreen® criteria classify chemicals as a Low hazard for respiratory sensitization when they are not GHS classified (CPA 2018b). The confidence in the score is low as this evaluation does not include non-immunologic mechanisms of respiratory sensitization, and no specific data are available for respiratory sensitization.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.
- OECD 2024
    - Ethyl lactate does not contain any structural alerts for respiratory sensitization (Appendix E).
- Based on the weight of evidence and guidance from ECHA regarding assessment of respiratory sensitization potential, a score of Low was assigned. The guidance from ECHA states that the mechanisms leading to respiratory sensitization are essentially similar to those leading to skin sensitization (ECHA 2017). ECHA recommended that if a chemical is not a dermal sensitizer based on high quality data, it is unlikely to be a respiratory sensitizer. ECHA also noted that this rationale does not cover respiratory hypersensitivity caused by non-immunological mechanisms, for which human experience is the main evidence of activity (ECHA 2017). As ethyl lactate was not sensitizing to the skin (see skin sensitization section above), and a literature search did not find any human evidence of respiratory sensitization by ethyl lactate, and as ethyl lactate does not contain any structural alerts for respiratory sensitization (OECD 2024), ethyl lactate is not expected to be a respiratory sensitizer.

Skin Irritation/Corrosivity (IrS) (Group II) Score (vH, H, M, or L): L
Ethyl lactate was assigned a score of Low for skin irritation/corrosivity based on a no dermal irritation effects seen in rabbits. GreenScreen® criteria classify chemicals as a Low hazard for skin irritation/corrosivity when adequate negative data are available and the chemical is not GHS classified (CPA 2018b). The confidence in the score is high as it is based on reliable experimental data on the target chemical.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #687-47-8, 2024
    - A GLP-compliant dermal irritation study was conducted according to OECD Guideline 404 in three male New Zealand White rabbits. Animals were administered 0.5 mL undiluted ethyl lactate (98% purity) to clipped skin under semi-occlusive dressings for 4 hours, with observations made at 1, 24, 48, and 72 hours, and 7 and 14 days post-treatment. There were no signs of erythema or edema seen up until 72 hours. While there was some scaliness seen

in two animals, this was attributed to the pressure of the bandage on the test patch. Based on the lack of effects, the study authors concluded that ethyl lactate was not dermally irritating (Klimisch 1, reliable without restrictions).

Eye Irritation/Corrosivity (IrE) (Group II) Score (vH, H, M, or L): vH
Ethyl lactate was assigned a score of Very High for eye irritation/corrosivity based on results in a GLP-compliant OECD Guideline 438 *in vitro/ex vivo* eye irritation study corresponding to a categorization of GHS Category 1, along with being associated with hazard statement H318 on both authoritative and screening lists. GreenScreen® criteria classify chemicals as a Very High hazard for eye irritation/corrosivity when classified as GHS Category 1 and associated with EU hazard statement H318 (CPA 2018b). The confidence in the score is high as it is based on reliable experimental data on the target chemical and an authoritative A list.

- Authoritative and Screening Lists
  - *Authoritative:*
    - EU GHS – H318 – Causes serious eye damage – Category 1
  - *Screening:*
    - Australia GHS – H318 – Causes serious eye damage – Category 1
    - New Zealand GHS – Serious eye damage category 1
- ECHA, CAS #687-47-8, 2024
  - In a GLP-compliant *in vitro* isolated chicken eye test similar to OECD Guideline 438 for identifying ocular corrosives and severe irritants, eyes were isolated from spring chickens. The 4 isolated eyes were exposed to 0.03 mL undiluted ethyl lactate (98% purity) for 10 seconds and observed for 4 hours. After treatment, the thickness of the cornea increased considerably, with a maximum mean corneal swelling of 31% seen at 4 hours post-treatment. Moderate to severe corneal opacity and severe fluorescein retention by damaged epithelial cells was seen, along with wrinkling of the corneal epithelium. Based on these effects, ethyl lactate is classified as a GHS Category 1 eye irritant (irreversible effects to the eyes (Klimisch 1, reliable without restrictions).

Ecotoxicity (Ecotox)

Acute Aquatic Toxicity (AA) Score (vH, H, M, or L): L
Ethyl lactate was assigned a score of Low for acute aquatic toxicity based on L/EC_{50} values of 320 mg/L in fish, 683 mg/L in daphnids, and 2,200 mg/L (based on growth rate) in algae. GreenScreen® criteria classify chemicals as a Low hazard for acute aquatic toxicity when L/EC_{50} values are >100 mg/L, adequate negative data are available, and the chemical is GHS not classified (CPA 2018b). The confidence in the score is high as it is based on reliable experimental data on the target chemical for all three trophic levels.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #687-47-8, 2024
  - 96-hour mortality LC_{50} in fish = 320 mg/L (*Danio rerio*, zebrafish, nominal) (GLP-compliant, OECD Guideline 203) (Klimisch 2, reliable with restrictions)
  - 48-hour mobility EC_{50} in daphnid = 683 mg/L (*Daphnia magna*, water flea, nominal) (GLP-compliant, OECD Guideline 202) (Klimisch 1, reliable without restrictions)

- 72-hour growth rate EC_{50} in algae = 2,200 mg/L, 72-hour biomass EC_{50} = 2,300 mg/L (*Raphidocelis subcapitata*, green algae, nominal) (GLP-compliant, OECD Guideline 201) (Klimisch 2, reliable with restrictions)

Chronic Aquatic Toxicity (CA) Score (vH, H, M, or L): *L*
Ethyl lactate was assigned a score of Low for chronic aquatic toxicity based on estimated chronic values of 35.38 mg/L in fish and 1,000.49 mg/L in daphnia and a measured chronic value of 320 mg/L in algae. GreenScreen® criteria classify chemicals as a Low hazard for chronic aquatic toxicity when chronic values are > 10 mg/L in all three trophic levels (CPA 2018b). The confidence in the score is low as it is in part based on modeled data.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #687-47-8, 2024
  - 72-hour growth rate NOEC in algae = 320 mg/L (*R. subcapitata*, green algae, nominal) (GLP-compliant, OECD Guideline 201) (Klimisch 2, reliable with restrictions)
- U.S. EPA 2022
  - Ethyl lactate belongs to the esters ECOSAR chemical class. The most conservative predicted chronic values (ChVs) are 35.38 mg/L in fish, 1,000.49 mg/L in daphnia, and 59.27 mg/L in green algae (Appendix F).

Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): *vL*
Ethyl lactate was assigned a score of Very Low for persistence based on the racemic mixture of ethyl lactate meeting the 10-day biodegradation window in an OECD Guideline 301F study, and based on its modeled dominant environmental compartments being soil and water. GreenScreen® criteria classify chemicals as a Very Low hazard for persistence when they meet the 10-day window in a ready biodegradation test when the dominant compartment is water, soil, or sediment (CPA 2018b). The confidence in the score is low due to the use of adapted inoculum, which would have optimized the inoculum to degrade the test substance faster.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #97-64-3, 2024
  - *Surrogate: Ethyl lactate (CAS #97-64-3):* In GLP-compliant ready biodegradability test conducted according to OECD Guideline 301F (Manometric Respirometry test), domestic, adapted activated sludge was exposed to ethyl lactate (purity not specified) at 62 mg/L for 28 days. At the end of the exposure period, the level of degradation was 70% based on O_2 consumption and the 10-day window was met with 61% degradation at the end of the 10-day window. The authors of the REACH dossier concluded that ethyl lactate was readily biodegradable in this study (Klimisch 1, reliable without restriction).
- U.S. EPA 2017
  - BIOWIN modeling of EPI Suite™ predicts that ethyl lactate is readily biodegradable. Fugacity modeling predicts that 52.6% will partition to soil with a half-life of 30 days, 43.7% to water with a half-life of 15 days, and 3.61% to air with a half-life of 65.8 hours (Appendix G).

Bioaccumulation (B) Score (vH, H, M, L, or vL): vL
Ethyl lactate was assigned a score of Very Low for bioaccumulation based on a measured log K_{ow} of 0.7 for the racemic mixture. GreenScreen® criteria classify chemicals as a Very Low hazard for bioaccumulation when log K_{ow} values are no greater than 4 (CPA 2018b). The confidence in the score is high as it is based on an experimental partition coefficient for a strong surrogate.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #97-64-3, 2024
  - *Surrogate: Ethyl lactate (CAS #97-64-3):* Log K_{ow} = 0.7 at 25°C (OECD Guideline 117, GLP-compliant) (Klimisch 1, reliable without restrictions)

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M, or L): *L*
Ethyl lactate was assigned a score of Low for reactivity based on the lack of structural alerts for oxidizing and explosive properties. GreenScreen® criteria classify chemicals as a Low hazard for reactivity when it does not warrant GHS classification for any of the reactivity sub-endpoints and the chemical is not present on authoritative or screening lists (CPA 2018b). The confidence in the score is low based on the lack of measured data on explosivity.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA, CAS #687-47-8, 2024
  - An explosiveness test and oxidizing liquid test are waived because ethyl lactate does not contain any functional groups associated with explosive or oxidizing properties.
- No measured data were identified. Therefore, screening procedures for explosivity were used here to estimate the reactivity property of ethyl lactate. These procedures are listed in the GHS (UN 2023).
  - Based on the structure of its components or moieties, ethyl lactate is not considered explosive or self-reactive due to lack of functional groups associated with explosive or self-reactive properties (See Appendix H).
  - Based on the structure of its components or moieties, ethyl lactate is not considered to have oxidizing properties as it does not contain any structural groups known to be correlated with a tendency to react exothermally with combustible materials. Specifically, organic substances which contain oxygen, fluorine, or chlorine where these elements are chemically bonded only to carbon or hydrogen, classification as an oxidizing liquid need not be applied. Therefore, as the molecular structure of ethyl lactate has 3 oxygens, which are all bonded only to carbon and hydrogen, classification is not warranted.

Flammability (F) Score (vH, H, M, or L): M
Ethyl lactate was assigned a score of Moderate for flammability based on a flash point of 53.4°C, which corresponds to GHS Category 3, as well as being listed on both authoritative and screening lists as GHS Category 3 with the hazard statement of H226. GreenScreen® criteria classify chemicals as a Moderate hazard for flammability when they are classified as GHS Category 3 or 4 flammable liquids (CPA 2018b). The confidence in the score is high as it is based on reliable experimental data and an authoritative A list.

- Authoritative and Screening Lists

  - *Authoritative:*
    - EU GHS – H226: Flammable liquid and vapor (Flammable liquids – Category 3)
  - *Screening:*
    - Australia GHS – H226: Flammable liquid and vapor (Flammable liquids – Category 3)
    - New Zealand GHS – Flammable liquids Category 3
- ECHA, CAS #687-47-8, 2024
  - In a GLP-compliant closed cup test conducted according to ISO 3679, a flash point of 53.4°C was established (Klimisch 1, reliable without restrictions).
    - According to GHS, a flash point ≥ 23°C and ≤ 60°C corresponds to GHS Category 3 (UN 2023).

Use of New Approach Methodologies (NAMs)[10] in the Assessment, Including Uncertainty Analyses of Input and Output

New Approach Methodologies (NAMs) used in this GreenScreen® include *in silico* modeling for endocrine activity, respiratory sensitization, and chronic aquatic toxicity, and *in vitro* testing for genotoxicity, endocrine activity, and eye irritation. NAMs are non-animal alternatives that can be used alone or in combination to provide information for safety assessment (Madden et al. 2020). At present, there is not a uniformly accepted framework on how to report and apply individual NAMs (U.S. EPA 2020, OECD 2020). The expanded application of NAMs greatly amplifies the need to communicate uncertainties associated with their use. As defined by EFSA (2018), uncertainty is "a general term referring to all types of limitations in available knowledge that affect the range and probability of possible answers to an assessment question." The quality, utility, and accuracy of NAM predictions are greatly influenced by two primary types of uncertainties (OECD 2020):

- Type I: Uncertainties related to the input data used
- Type II: Uncertainties related to extrapolations made

As shown in Table 4, Type I (input data) uncertainties in ethyl lactate's NAMs dataset include lack of sufficient data for endocrine activity, respiratory sensitization, eye irritation, and chronic aquatic toxicity, and lack of validated test methods for respiratory sensitization. Ethyl lactate's Type II (extrapolation output) uncertainties include the lack of a defined applicability domain of OECD Toolbox structural alerts and ToxCast models, limitations of *in vitro* genotoxicity tests in mimicking *in vivo* metabolism and their focusing on only a few events in genotoxicity, unclear *in vivo* relevance of *in vitro* receptor binding activity assays due to lack of consideration of toxicokinetics, incomplete coverage of endocrine pathways in the Tox21 EDSP program, inability of single *in vitro* skin or eye tests to determine GHS classifications, and lack of consideration of non-immunological mechanisms of respiratory sensitization. Some of ethyl lactate's type II uncertainties were alleviated by the use of *in vitro* test batteries and/or in combination of *in vivo* data.

Table 4: Summary of NAMs Used in the GreenScreen® Assessment, Including Uncertainty Analyses

Uncertainty Analyses (OECD 2020)	
Type I Uncertainty: Data/Model Input	**Endocrine activity:** Insufficient data are available on circulating hormones for some pathways. **Respiratory sensitization**: No experimental data are available and there are no validated test methods. **Eye irritation:** No *in vivo* data were identified. **Chronic aquatic toxicity:** No data were identified for fish and daphnia trophic levels
Type II Uncertainty: Extrapolation Output	**Genotoxicity:** The bacterial reverse mutation assay (as defined in OECD Guideline 471) only tests point-mutation inducing activity in non-mammalian cells, and the exogenous metabolic activation system does not entirely mimic *in vivo* conditions[11]. The

[10] NAMs refers to any non-animal technology, methodology, approach, or combination thereof that inform chemical hazard and risk assessments. NAMs include *in silico*/computational tools, *in vitro* biological profiling (e.g., cell cultures, 2,3-D organotypic culture systems, genomics/transcriptomics, organs on a chip), and frameworks (i.e., adverse outcome pathways (AOPs), defined approaches (DA), integrated approaches to testing and assessment (IATA).

[11] https://www.oecd-ilibrary.org/docserver/9789264071247-en.pdf?expires=1614097593&id=id&accname=guest&checksum=89925F80B9F4BD2FFC6E90F94A0EE427

	mammalian cell gene mutation assay (as defined in OECD Guideline 476) only detects gene mutations, and the exogenous metabolic activation system does not entirely mirror *in vivo* metabolism (i.e., the liver S9 mix contains enzymes present in the endoplasmic reticulum but not the cytosol of liver cells).[12] The *in vitro* chromosome aberration assay (OECD Guideline 473) does not measure aneuploidy and it only measures structural chromosomal aberrations. The exogenous metabolic activation system does not entirely mirror *in vivo* metabolism[13]. **Endocrine activity:** ToxCast models don't define applicability domain; the *in vivo* relevance of EDSP Tox 21 screening assays is unknown due to lack of consideration of metabolism and other toxicokinetic factors. EDSP Tox 21 assays do not cover all critical endocrine pathways. **Respiratory sensitization**: The OECD Toolbox only identifies structural alerts, and does not define applicability domains. Additionally, the ECHA guidance (2017), on which the use of OECD Toolbox structural alerts is based, does not evaluate non-immunologic mechanisms for respiratory sensitization. **Eye irritation**: The OECD Guideline 438 test method could not be used to identify chemicals that are irritating to the eyes (i.e., GHS Categories 2A and 2B). As it uses enucleated chicken eyes, it is not a true non-animal test[14].	
Endpoint	**NAMs Data Available and Evaluated? (Y/N)**	**Types of NAMs Data (*in silico* modeling/*in vitro* biological profiling/frameworks)**
Carcinogenicity	N	
Mutagenicity	Y	*In vitro* data: Bacterial reverse mutation assay/*in vitro* gene mutation assay/*in vitro* chromosome aberration assay
Reproductive toxicity	N	
Developmental toxicity	N	
Endocrine activity	Y	*In vitro* high throughput data: EDSP Tox 21 screening assays *In silico* modeling: ToxCast
Acute mammalian toxicity	N	
Single exposure systemic toxicity	N	
Repeated exposure systemic toxicity	N	

[12] https://www.oecd-ilibrary.org/docserver/9789264264809-en.pdf?expires=1614097800&id=id&accname=guest&checksum=C0DE371FB9C5A878E66C9AB7F84E6BBE
[13] https://www.oecd-ilibrary.org/docserver/9789264264649-en.pdf?expires=1614098015&id=id&accname=guest&checksum=6A4F9CE52EA974F5A74793DD54D54352
[14] https://www.oecd-ilibrary.org/docserver/9789264203860-en.pdf?expires=1657729772&id=id&accname=guest&checksum=05C34780720727D92856887CAD43C8DD

Single exposure neurotoxicity	N	
Repeated exposure neurotoxicity	N	
Skin sensitization	N	
Respiratory sensitization	Y	*In silico* modeling: OECD Toolbox structural alerts
Skin irritation	N	
Eye irritation	Y	*In vitro* test: OECD Guideline 438 Test
Acute aquatic toxicity	N	
Chronic aquatic toxicity	Y	*In silico* modeling: ECOSAR
Persistence	Y	*In silico* modeling: EPI Suite™ Non-animal testing: OECD 301F ready biodegradability test
Bioaccumulation	N	

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APPENDIX A: Hazard Classification Acronyms
(in alphabetical order)

(AA) Acute Aquatic Toxicity

(AT) Acute Mammalian Toxicity

(B) Bioaccumulation

(C) Carcinogenicity

(CA) Chronic Aquatic Toxicity

(D) Developmental Toxicity

(E) Endocrine Activity

(F) Flammability

(IrE) Eye Irritation/Corrosivity

(IrS) Skin Irritation/Corrosivity

(M) Mutagenicity and Genotoxicity

(N) Neurotoxicity

(P) Persistence

(R) Reproductive Toxicity

(Rx) Reactivity

(SnS) Sensitization- Skin

(SnR) Sensitization- Respiratory

(ST) Systemic/Organ Toxicity

APPENDIX B: Results of Automated GreenScreen® Score Calculation for Ethyl Lactate (CAS #687-47-8)

TOXSERVICES
TOXICOLOGY RISK ASSESSMENT CONSULTING

GREEN SCREEN FOR SAFER CHEMICALS

GreenScreen® Score Inspector

Table 1: Hazard Table

			Group I Human					Group II and II* Human								Ecotox		Fate		Physical	
			Carcinogenicity	Mutagenicity/Genotoxicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
Table 2: Chemical Details									S	R *	S	R *	*	*								
Inorganic Chemical?	Chemical Name	CAS#	C	M	R	D	E	AT	STs	STr	Ns	Nr	SNS*	SNR*	IrS	IrE	AA	CA	P	B	Rx	F
No	Ethyl lactate	687-47-8	L	L	*L*	*M*	*M*	L	M	L	*M*	L	L	*L*	L	vH	L	*L*	*vL*	vL	*L*	M

Table 3: Hazard Summary Table

Benchmark	a	b	c	d	e	f	g
1	No	No	No	No	No		
2	No	No	No	No	Yes	Yes	No
3	STOP						
4	STOP						

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
Ethyl lactate	2

Note: Chemical has not undergone a data gap assessment. Not a Final GreenScreen™ Score

Table 6

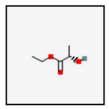
Chemical Name	Final GreenScreen® Benchmark Score
Ethyl lactate	2

After Data gap Assessment
Note: No Data gap Assessment Done if Preliminary GS Benchmark Score is 1.

Table 5: Data Gap Assessment Table

Datagap Criteria	a	b	c	d	e	f	g	h	i	j	bm4	End Result
1												
2	Yes	Yes	Yes	Yes	Yes							2
3												
4												

APPENDIX C: Pharos Output for Ethyl Lactate (CAS #687-47-8)



687-47-8

(L)-(-)-Ethyl lactate

ALSO CALLED (L)-(-)-Ethyl lactate, (L)-Ethyl lactate, 13171-69-2, 211-694-1, DTXSID9042336, Propanoic acid, 2-hy...

View all synonyms (6)

SHARE PROFILE

HAZARDS | PROPERTIES | FUNCTIONAL USES | RESOURCES

All Hazards View

Show PubMed Results | REQUEST ASSESSMENT | ADD TO COMPARISON

		Group I Human					Group II and II* Human								Ecotox			Fate		Physical		Mult	Non-GSLT			
	GREENSCREEN®	C	M	R	D	E	AT	ST	ST	N	N	SnS	SnR	IrS	IrE	AA	CA	ATB	P	B	Rx	F	Mult	PBT	GW	O	Other
List Hazard Summary	LT-UNK	-	-	-	-	-	-	M	-	-	-	-	-	pC	vH	-	-	-	-	-	-	M	M	-	-	-	R

Hazard Lists

DOWNLOAD LISTS

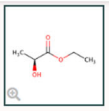
ENDPOINT	HAZARD LEVEL	GREENSCREEN®	LIST NAME	HAZARD DESCRIPTION	OTHER LISTS
Systemic Toxicity/Organ Effects-Single Exposure	M	LT-UNK	EU - GHS (H-Statements) Annex 6 Table 3-1	H335 - May cause respiratory irritation [Specific target organ toxicity - single exposure; Respiratory tract irritation - Category 3]	+2
	M	LT-UNK	GHS - Australia	H335 - May cause respiratory irritation [Specific target organ toxicity - single exposure; Respiratory tract irritation - Category 3]	
	pC	NoGS	EU - Manufacturer REACH hazard submissions	H335 - May cause respiratory irritation (unverified) [Specific target organ toxicity - single exposure; Respiratory tract irritation - Category 3]	
Skin Irritation/Corrosivity	pC	NoGS	EU - Manufacturer REACH hazard submissions	H315 - Causes skin irritation (unverified) [Skin corrosion/irritation - Category 2]	

Eye Irritation/Corrosivity	vH	LT-UNK	EU - GHS (H-Statements) Annex 6 Table 3-1	H318 - Causes serious eye damage [Serious eye damage/eye irritation - Category 1]	+3
	vH	LT-UNK	GHS - Australia	H318 - Causes serious eye damage [Serious eye damage/eye irritation - Category 1]	
	vH	LT-UNK	GHS - New Zealand	Serious eye damage category 1	
	pC	NoGS	EU - Manufacturer REACH hazard submissions	H318 - Causes serious eye damage (unverified) [Serious eye damage/eye irritation - Category 1]	
Flammability	M	LT-UNK	EU - GHS (H-Statements) Annex 6 Table 3-1	H226 - Flammable liquid and vapour [Flammable liquids - Category 3]	+3
	M	LT-UNK	GHS - Australia	H226 - Flammable liquid and vapour [Flammable liquids - Category 3]	
	M	LT-UNK	GHS - New Zealand	Flammable liquids category 3	
	pC	NoGS	EU - Manufacturer REACH hazard submissions	H226 - Flammable liquid and vapour (unverified) [Flammable liquids - Category 3]	
Systemic Toxicity/Organ Effects [Single Exposure] and/or Neurotoxicity [Single Exposure]	M	LT-UNK	GHS - New Zealand	Specific target organ toxicity - single exposure category 3 narcotic effects	
Human and/or Aquatic toxicity and/or Persistence and/or Bioaccumulation	U	LT-UNK	German FEA - Substances Hazardous to Waters	Class 1 - Low Hazard to Waters	

Restricted Substance Lists (3)

- EU - PACT-RMOA Substances: Substances selected for RMOA or hazard assessment
- Food Contact Chemicals Database (FCCdb): Food Contact Chemicals Database Version 5.0
- TSCA Chemical Substance Inventory (Active-Inactive): TSCA Commercially Active

APPENDIX D: U.S. EPA's EDSP21 and ToxCast Results for Ethyl Lactate (CAS #687-47-8)



(L)-(-)-Ethyl lactate
687-47-8 | DTXSID9042336
Searched by CASRN

Bioactivity - ToxCast: Models

EXPORT

ToxCast Model Predictions

Model	Receptor	Agonist	Antagonist	Binding
CERAPP Potency Level (From Literature)	Estrogen	Inactive	Inactive	Inactive
CERAPP Potency Level (Consensus)	Estrogen	0.00	0.00	0
COMPARA (Consensus)	Androgen	0.00	0.00	0

EXPORT

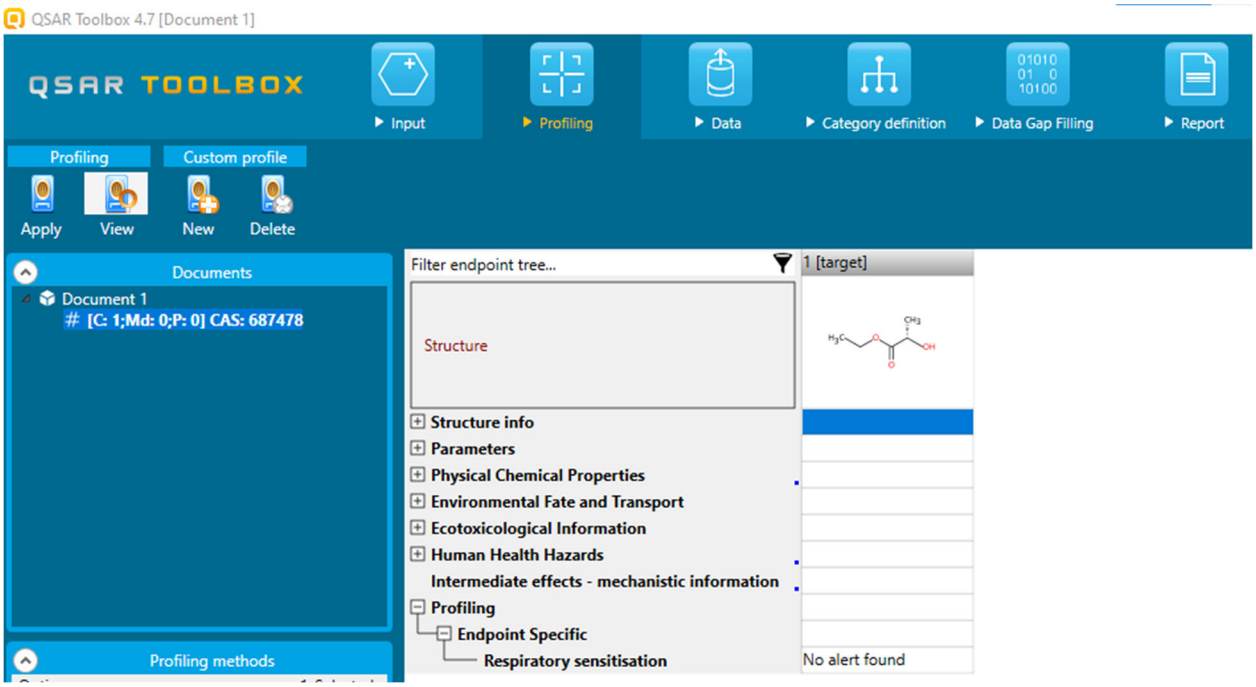
Bioactivity Summary Grid

Filter out non-representative sample (Repr.) results

Filter out 'background' from Intended Target Family

Name	Assay Lists	Details	SeqAPASS	Gene Symbol	AOP	Event	Repr. Plot	All Plots	Hit Call	Continuous Hit Call	Top	AC50	logAC50	Cutoff	AC
	(3) EDSP AR,EDSP														
TOX21_AR_LUC_MDAKB2_Ant	EDSP_AR		P10275.3	AR	-	-			Inactive	0	1.36e-9	45.00	1.65	32.13	
ATG_AR_TRANS	EDSP_AR		P10275.3	AR	-	-			Inactive	0	0.10	100.00	2.00	0.86	
ATG_ERE_CIS	EDSP_ER		NP_000116.2	ESR1	-	-			Inactive	0	-1.30e-2	100.00	2.00	0.50	
ACEA_ER_80hr	EDSP_ER		NP_000116.2	ESR1	220	1394			Inactive	0	3.80	1.49	0.17	25.49	
ATG_ERa_TRANS	EDSP_ER		NP_000116.2	ESR1	-	-			Inactive	0	7.53e-14	100.00	2.00	1.10	
TOX21_TSHR_HTRF_Antagoni	EDSP_thyroid		P16473.2	TSHR	42 | 54 | 159	277			Inactive	-	2.34	45.00	1.65	20.00	
ATG_THRa1_TRANS	EDSP_thyroid		NP_003242.1	THRA	-	-			Inactive	0	8.72e-12	100.00	2.00	1.10	
TOX21_TRHR_HEK293_antago	EDSP_thyroid			TRHR	48	389			Inactive	-	1.11e-9	30.00	1.48	20.00	
TOX21_TRHR_HEK293_agonis	EDSP_thyroid			TRHR	48	389			Inactive	-	1.47e-11	30.00	1.48	20.00	
TOX21_TSHR_HTRF_Agonist_	EDSP_thyroid		P16473.2	TSHR	42 | 54 | 159	277			Inactive	0	3.83e-9	45.00	1.65	27.85	
TOX21_TSHR_wt_Agonist_HTF	EDSP_thyroid		P16473.2	TSHR	-	-			Inactive	0	2.56	45.00	1.65	20.00	
TOX21_AR_LUC_MDAKB2_Ant	cytotoxicity_burst EDSP_AR				263	1771			Inactive	-	2.48e-11	45.00	1.65	20.00	
ACEA_ER_AUC_viability	cytotoxicity_burst EDSP_ER				220 | 263	1394 | 1821			Inactive	0.2668	19.80	50.00	1.70	20.00	

APPENDIX E: OECD Toolbox Respiratory Sensitization Results for Ethyl Lactate (CAS #687-47-8)



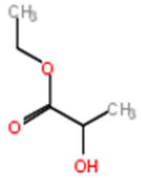
APPENDIX F: ECOSAR Modeling Results for Ethyl Lactate (CAS #687-47-8)

Organic Module Report

Results of Organic Module Evaluation

CAS	Name	SMILES
687478		OC(C)C(=O)OCC

Structure



Details	
Mol Wt	118.13
Selected LogKow	-0.18
Selected Water Solubility (mg/L)	1000000
Selected Melting Point (°C)	-9
Estimated LogKow	-0.18
Estimated Water Solubility (mg/L)	986538.31
Measured LogKow	
Measured Water Solubility (mg/L)	1000000
Measured Melting Point (°C)	

Class Results:	

Esters

Organism	Duration	End Point	Concentration (mg/L)	Max Log Kow	Flags
Fish	96h	LC50	297.4	5	
Daphnid	48h	LC50	781.01	5	
Green Algae	96h	EC50	469.73	6.4	
Fish		ChV	35.38	8	
Daphnid		ChV	1000.49	8	
Green Algae		ChV	59.27	8	
Fish (SW)	96h	LC50	517.15	5	
Mysid	96h	LC50	1491.34	5	

APPENDIX G: EPI Suite™ Modeling Results for Ethyl Lactate (CAS #687-47-8)

CAS Number: 000097-64-3
SMILES : OC(C)C(=O)OCC
CHEM : ETHYL LACTATE
MOL FOR: C5 H10 O3
MOL WT : 118.13
---------- EPI SUMMARY (v4.11) ----------
Physical Property Inputs:
Log Kow (octanol-water): ------
Boiling Point (deg C) : 154.00
Melting Point (deg C) : -9.00
Vapor Pressure (mm Hg) : 3.75
Water Solubility (mg/L): 1E+006
Henry LC (atm-m3/mole) : ------

Log Octanol-Water Partition Coef (SRC):
Log Kow (KOWWIN v1.69 estimate) = -0.18

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
Boiling Pt (deg C): 166.19 (Adapted Stein & Brown method)
Melting Pt (deg C): -27.76 (Mean or Weighted MP)
VP(mm Hg,25 deg C): 1.08 (Mean VP of Antoine & Grain methods)
VP (Pa, 25 deg C) : 144 (Mean VP of Antoine & Grain methods)
BP (exp database): 154 deg C
VP (exp database): 3.75E+00 mm Hg (5.00E+002 Pa) at 25 deg C

Water Solubility Estimate from Log Kow (WSKOW v1.42):
Water Solubility at 25 deg C (mg/L): 9.865e+005
log Kow used: -0.18 (estimated)
melt pt used: -9.00 deg C
Water Sol (Exper. database match) = 1e+006 mg/L (20 deg C)
Exper. Ref: YALKOWSKY,SH & DANNENFELSER,RM (1992)

Water Sol Estimate from Fragments:
Wat Sol (v1.01 est) = 6.173e+005 mg/L

ECOSAR Class Program (ECOSAR v1.11):
Class(es) found:
Esters

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
Bond Method : 4.82E-005 atm-m3/mole (4.88E+000 Pa-m3/mole)
Group Method: Incomplete
Exper Database: 5.83E-07 atm-m3/mole (5.91E-002 Pa-m3/mole)
For Henry LC Comparison Purposes:
User-Entered Henry LC: not entered
Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:
HLC: 5.829E-007 atm-m3/mole (5.906E-002 Pa-m3/mole)

VP: 3.75 mm Hg (source: User-Entered)
WS: 1E+006 mg/L (source: User-Entered)

Log Octanol-Air Partition Coefficient (25 deg C) [KOAWIN v1.10]:
Log Kow used: -0.18 (KowWin est)
Log Kaw used: -4.623 (exp database)
Log Koa (KOAWIN v1.10 estimate): 4.443
Log Koa (experimental database): None

Probability of Rapid Biodegradation (BIOWIN v4.10):
Biowin1 (Linear Model) : 1.0242
Biowin2 (Non-Linear Model) : 0.9985
Expert Survey Biodegradation Results:
Biowin3 (Ultimate Survey Model): 3.2383 (weeks)
Biowin4 (Primary Survey Model) : 4.0357 (days)
MITI Biodegradation Probability:
Biowin5 (MITI Linear Model) : 0.7764
Biowin6 (MITI Non-Linear Model): 0.9108
Anaerobic Biodegradation Probability:
Biowin7 (Anaerobic Linear Model): 0.8417
Ready Biodegradability Prediction: YES

Hydrocarbon Biodegradation (BioHCwin v1.01):
Structure incompatible with current estimation method!

Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:
Vapor pressure (liquid/subcooled): 500 Pa (3.75 mm Hg)
Log Koa (Koawin est): 4.443
Kp (particle/gas partition coef. (m3/ug)):
Mackay model : 6E-009
Octanol/air (Koa) model: 6.81E-009
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model : 2.17E-007
Mackay model : 4.8E-007
Octanol/air (Koa) model: 5.45E-007

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant = 4.0739 E-12 cm3/molecule-sec
Half-Life = 2.626 Days (12-hr day; 1.5E6 OH/cm3)
Half-Life = 31.506 Hrs
Ozone Reaction:
No Ozone Reaction Estimation
Fraction sorbed to airborne particulates (phi):
3.48E-007 (Junge-Pankow, Mackay avg)
5.45E-007 (Koa method)
Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (KOCWIN v2.00):

Koc : 1 L/kg (MCI method)
Log Koc: 0.000 (MCI method)
Koc : 2.231 L/kg (Kow method)
Log Koc: 0.348 (Kow method)

Aqueous Base/Acid-Catalyzed Hydrolysis (25 deg C) [HYDROWIN v2.00]:
Total Kb for pH > 8 at 25 deg C : 1.117E+000 L/mol-sec
Kb Half-Life at pH 8: 7.179 days
Kb Half-Life at pH 7: 71.793 days
(Total Kb applies only to esters, carbmates, alkyl halides)

Bioaccumulation Estimates (BCFBAF v3.01):
Log BCF from regression-based method = 0.500 (BCF = 3.162 L/kg wet-wt)
Log Biotransformation Half-life (HL) = -2.3952 days (HL = 0.004026 days)
Log BCF Arnot-Gobas method (upper trophic) = -0.043 (BCF = 0.9057)
Log BAF Arnot-Gobas method (upper trophic) = -0.043 (BAF = 0.9057)
log Kow used: -0.18 (estimated)

Volatilization from Water:
Henry LC: 5.83E-007 atm-m3/mole (Henry experimental database)
Half-Life from Model River: 1093 hours (45.53 days)
Half-Life from Model Lake : 1.201E+004 hours (500.4 days)

Removal In Wastewater Treatment:
Total removal: 1.88 percent
Total biodegradation: 0.09 percent
Total sludge adsorption: 1.76 percent
Total to Air: 0.03 percent
(using 10000 hr Bio P,A,S)

Level III Fugacity Model: (MCI Method)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	**3.61**	**65.8**	**1000**
Water	**43.7**	**360**	**1000**
Soil	**52.6**	**720**	**1000**
Sediment	**0.0818**	**3.24e+003**	**0**

Persistence Time: 396 hr

Level III Fugacity Model: (MCI Method with Water percents)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	3.61	65.8	1000
Water	43.7	360	1000
water	(43.7)		
biota	(1.44e-006)		
suspended sediment	(6.55e-005)		
Soil	52.6	720	1000
Sediment	0.0818	3.24e+003	0

Persistence Time: 396 hr

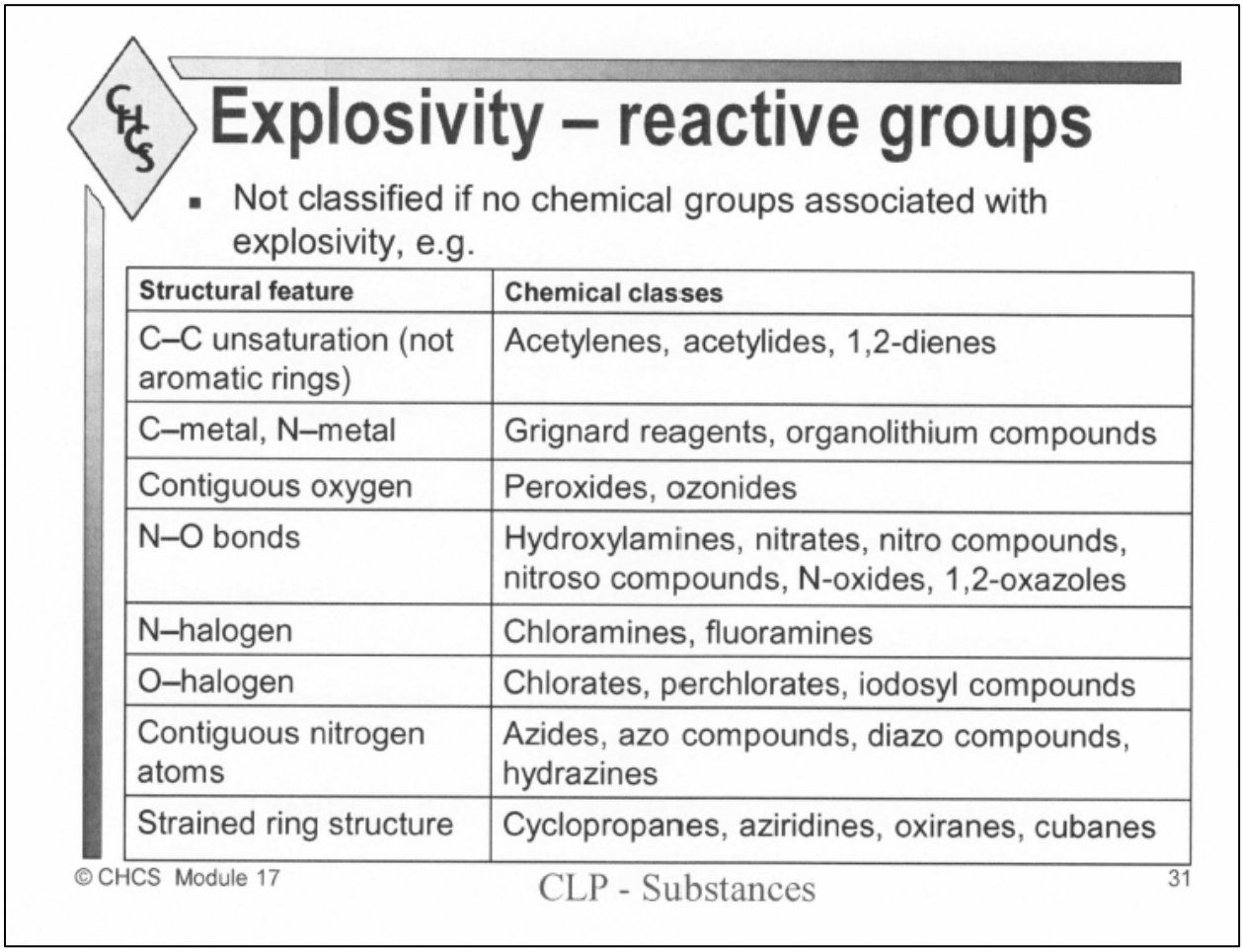
Level III Fugacity Model: (EQC Default)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	3.65	65.8	1000
Water	44.5	360	1000
water	(44.5)		
biota	(1.47e-006)		
suspended sediment	(1.81e-005)		
Soil	51.7	720	1000
Sediment	0.082	3.24e+003	0

Persistence Time: 392 hr

APPENDIX H: Known Structural Alerts for Reactivity

Explosivity – Abbreviated List



Explosivity – reactive groups

- Not classified if no chemical groups associated with explosivity, e.g.

Structural feature	Chemical classes
C–C unsaturation (not aromatic rings)	Acetylenes, acetylides, 1,2-dienes
C–metal, N–metal	Grignard reagents, organolithium compounds
Contiguous oxygen	Peroxides, ozonides
N–O bonds	Hydroxylamines, nitrates, nitro compounds, nitroso compounds, N-oxides, 1,2-oxazoles
N–halogen	Chloramines, fluoramines
O–halogen	Chlorates, perchlorates, iodosyl compounds
Contiguous nitrogen atoms	Azides, azo compounds, diazo compounds, hydrazines
Strained ring structure	Cyclopropanes, aziridines, oxiranes, cubanes

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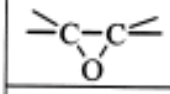
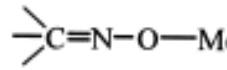
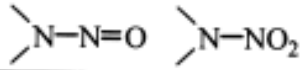
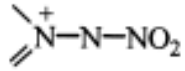
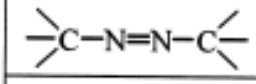
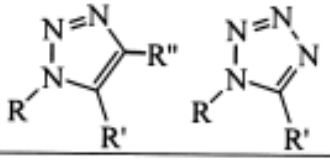
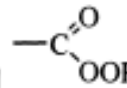
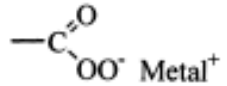
Explosivity – Full List

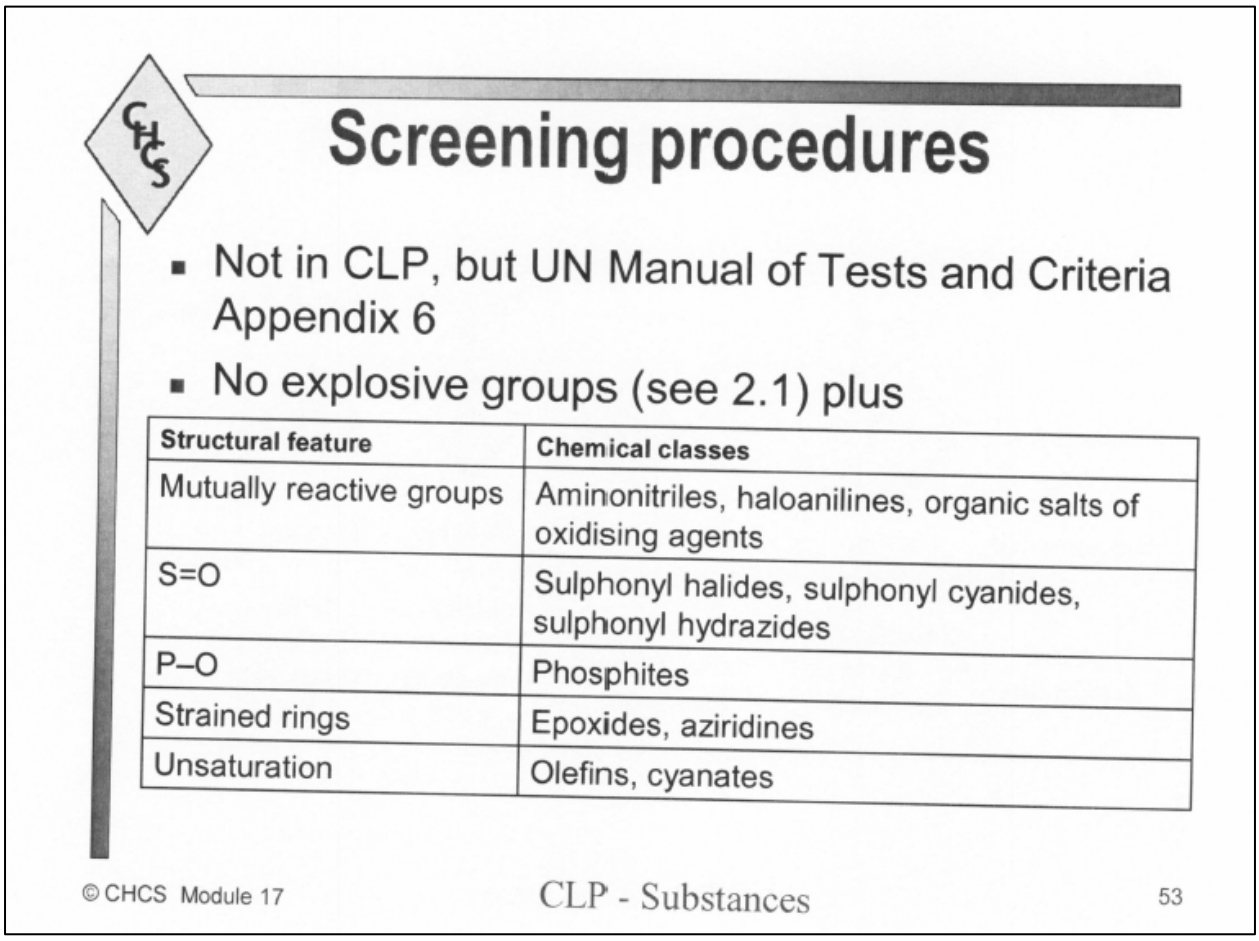
Table R.7.1-28 Chemical groups associated with explosive properties

Chemical group	Chemical Class
-C≡C- -C≡C-Metal -C≡C-Halogen	Acetylenic Compounds Metal Acetylides Haloacetylene Derivatives
	Diazo Compounds
-N=O -NO_2	Nitroso and Nitro Compounds,
R-O-N=O R-O-NO_2	Acyl or Alkyl Nitrites and Nitrates
	1,2-Epoxides
	Metal Fulminates or *aci*-Nitro Salts
	N-Metal Derivatives (especially heavy metals)
	N-Nitroso and N-Nitro Compounds
	N-Azolium Nitroimidates
	Azo Compounds
Ar-N=N-O-Ar	Arene Diazoates
$(ArN=N)_2O$, $(ArN=N)_2S$	Bis-Arenediazo Oxides and Sulfides
RN=N-NR'R''	Triazines
	High-nitrogen Compounds: e.g. Triazoles, Tetrazoles

Chemical group	Chemical Class
[1] ROOR', [2] 	Peroxy Compounds: [1] Alkyl hydroperoxides (R'=H), Peroxides (R'=organic); [2] Peroxo acids (R'=H), Peroxyesters (R'=organic)
[1] ROOMetal, [2] 	Metal peroxides, Peroxoacids salts
$-N_3$	Azides e.g. PbN_6, CH_3N_3
$^{-}O-C-N_2^{+}$	Arenediazonium oxides i.e. inner diazonium salts in which the counter ion is an oxide
Ar-N=N-S- Ar-N=N-S-Ar	Diazonium sulfides and derivatives, Arenediazo Aryl Sulfides
XO_n	Halogen Oxide: e.g. percholrates, bromates, etc
NX_3 e.g. $NC1_3$, $RNC1_2$	N-Halogen Compounds

Adapted from Bretherick (Bretherick's Handbook of Reactive Chemical Hazards 6th Ed., 1999, Butterworths, London)

Self-Reactive Substances



APPENDIX I: Change in Benchmark Score

Table 5 provides a summary of changes to the GreenScreen® Benchmark™ for ethyl lactate. The original GreenScreen® assessment was performed in 2024 with minor revisions in 2025 under version 1.4 criteria and ToxServices assigned a Benchmark 2 (BM-2) score.

Table 5: Change in GreenScreen® Benchmark™ for Ethyl Lactate

Date	GreenScreen® Benchmark™	GreenScreen® Version	Comment
December 19, 2024	BM-2	v. 1.4	Original GreenScreen® assessment.
February 24, 2025	BM-2	v. 1.4	No change in benchmark score. Confidence level for persistence score is corrected from high to low. Additional minor edits were made to address comments from Washington Department of Ecology.

Licensed GreenScreen® Profilers

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