CAPRYLYL GLYCOL

(CAS #1117-86-8)

GREENSCREEN® FOR SAFER CHEMICALS (GREENSCREEN®) ASSESSMENT

Prepared by:

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Assessment Date: March 18, 2024

Expiration Date: March 18, 2029

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GreenScreen® Executive Summary for Caprylyl Glycol (CAS #1117-86-8)

Caprylyl glycol is a fatty alcohol. It is used in cosmetic formulations as a preservative, skin and hair conditioning agent, and a viscosity agent, and in a variety of industrial and consumer products as an emollient, preservative, antioxidant, and solvent. Caprylyl glycol is a liquid at room temperature. While it has good solubility in water, its stability in water is not well characterized and it is unclear at which concentration it begins to form micelles, which is a challenge for assessing its aquatic toxicity. Caprylyl glycol has a boiling point of 267°C, and a low vapor pressure of 0.28 Pa; therefore, it is not a volatile organic compound (VOC).

Caprylyl glycol 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 Health (developmental toxicity-D)

A data gap (DG) exists for endocrine activity-E. As outlined in GreenScreen® Guidance Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis), caprylyl glycol meets requirements for a GreenScreen Benchmark™ Score of 2 despite the hazard data gap. In a worst-case scenario, if caprylyl glycol were assigned a High score for the data gap E, it would be categorized as a Benchmark 1 Chemical.

The GreenScreen® Benchmark Score for caprylyl glycol has changed over time. The original GreenScreen® assessment was performed in 2015 under version 1.2 criteria and ToxServices assigned a Benchmark 3 (BM-3) score. Most recently in 2024, ToxServices changed the GreenScreen® benchmark score to a BM-2 due to new data and reclassification of the developmental toxicity endpoint. The rating changed from a **Low** (high confidence) based on surrogate data, to a *Moderate* (low confidence) based on data for the target compound.

New Approach Methodologies (NAMs) used in this GreenScreen® include *in silico* modeling for carcinogenicity, endocrine activity, respiratory sensitization, and chronic aquatic toxicity, and *in vitro* data for mutagenicity, 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 caprylyl glycol's NAMs dataset include limited data for carcinogenicity, genotoxicity, endocrine activity, and chronic aquatic toxicity, and neither experimental data nor available validated test methods for respiratory sensitization. Caprylyl glycol's Type II (extrapolation output) uncertainties include use of structural alerts and modeling programs without defined applicability domains, reliance on *in vitro* assays to assess genotoxicity where the methods do not fully mimic *in vivo* metabolic conditions and only focus on a few events of the genotoxicity process, the uncertain *in vivo* relevance of *in silico* modeling and *in vitro* high throughput screening assays due to lack of consideration of toxicokinetics. the lack of consideration of non-immunologic mechanisms for respiratory sensitization when evaluating the structural alerts and the limitation of the hen's egg test-chorioallantoic membrane (HET-CAM) in identifying irritating substances that are not corrosive. Some of caprylyl glycol's type II uncertainties were alleviated by the use of *in vitro* test batteries and/or in combination of *in vivo* data.

GreenScreen® Hazard Summary Table for Caprylyl Glycol

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*	DG	**L**	**L**	**L**	**M**	**L**	**L**	*L*	**L**	**H**	*M*	*M*	**vL**	**vL**	*L*	**L**

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 Caprylyl Glycol (CAS #1117-86-8)

Method Version: GreenScreen® Version 1.4
Assessment Type[1]: Certified
Assessor Type: Licensed GreenScreen® Profiler

GreenScreen® Assessment (v.1.2) Prepared By:
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Date: April 7, 2015

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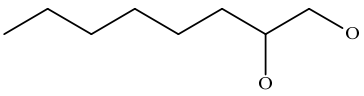
Organization: ToxServices LLC
Date: February 22, 2024; March 18, 2024

Expiration Date: March 18, 2029[2]

Chemical Name: Caprylyl glycol

CAS Number: 1117-86-8



Caprylyl glycol (CAS # 1117-86-8) (PubChem 2024)

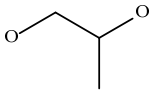
Also called: 1,2-Octanediol; Octane-1,2-diol (IUPAC); 1,2-Dihydroxyoctane; EC 214-254-7 (PubChem 2024)

Suitable surrogates or moieties of chemicals used in this assessment (CAS #'s):
Caprylyl glycol has a relatively complete toxicological dataset. The Cosmetics Ingredient Review (CIR) Expert Panel reviewed a number of 1,2 glycol compounds, including caprylyl glycol in a group as these chemicals have similar structures and physicochemical properties, and therefore are expected to have similar toxicities (CIR 2012). Each of these compounds has a hydroxyl group (-OH) on the first and second carbons and varies only by the number of carbons. For the carcinogenicity endpoint, ToxServices performed modeling and used data on the C3 glycol (propylene glycol), as it is the only group member with data.

For the aquatic toxicity endpoint, ToxServices considered data for slightly shorter and longer-chained 1,2-glycols, 1,2-Pentanediol (CAS #5343-92-0) and 1,2-Decanediol (CAS #1119-86-4).

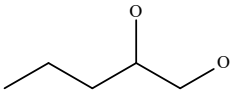
[1] GreenScreen® reports are either "UNACCREDITED" (by unaccredited person), "AUTHORIZED" (by Authorized GreenScreen® Practitioner), or "CERTIFIED" (by Licensed GreenScreen® Profiler or equivalent).
[2] Assessments expire five years from the date of completion starting from January 1, 2019. An assessment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

Surrogate #1:



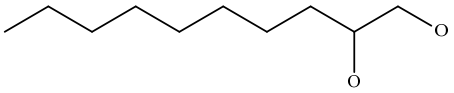
Propylene glycol (CAS #57-55-6) (PubChem 2024)

Surrogate #2:



1,2-Pentanediol (CAS #5343-92-0) (PubChem 2024)

Surrogate #3:



1,2-Decanediol (CAS #1119-86-4) (PubChem 2024)

Identify Applications/Functional Uses:

1. Emollient, humectant, and hair and skin conditioning agent in personal care product formulations at 0.00003 to 5% (CIR 2012).
2. Preservative in personal care product formulations at 0.00003 to 5% (CIR 2012).
3. Emollient, preservative, antioxidant, and solvent (U.S. EPA 2024a).

Known Impurities[3]:

No information is available. The screen is performed on the theoretical pure substance.

GreenScreen® Summary Rating for Caprylyl Glycol[4,5 6,7]: Caprylyl glycol 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 Health (developmental toxicity-D)

A data gap (DG) exists for endocrine activity-E. As outlined in GreenScreen® Guidance Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis) (CPA 2018b), caprylyl glycol meets requirements for a GreenScreen Benchmark™ Score of 2 despite the hazard data gap. In a worst-case scenario, if caprylyl glycol were assigned a High score for the data gap E, it would be categorized as a Benchmark 1 Chemical.

[3] Impurities of the chemical will be assessed at the product level instead of in this GreenScreen®.
[4] 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.
[5] See Appendix A for a glossary of hazard endpoint acronyms.
[6] For inorganic chemicals only, see GreenScreen® Guidance v1.4 Section 12 (Inorganic Chemical Assessment Procedure).
[7] 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.

Figure 1: GreenScreen® Hazard Summary Table for Caprylyl Glycol

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*	DG	L	L	L	**M**	L	L	*L*	L	**H**	*M*	*M*	**vL**	**vL**	*L*	L

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.

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 caprylyl glycol is readily biodegradable, it is not expected to have relevant transformation products.

Introduction

Caprylyl glycol, also called 1,2-octanediol, is a C8 fatty alcohol that belongs to the class of 1,2-glycols. The 1,2-gycols have a hydroxyl group (-OH) on the first and second carbons and vary only by the number of carbon atoms. These compounds are often produced by catalytic oxidation of alkene oxides, or by reduction of 2-hydroxy acids (CIR 2012).

ToxServices assessed caprylyl glycol 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 2015). Caprylyl glycol is on the SCIL with a full green circle, indicating it has been verified to be of low concern (U.S. EPA 2024a).

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),[8] 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 caprylyl glycol can be found in Appendix C.

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

- Caprylyl glycol is an LT-UNK (Benchmark score Unknown) chemical when screened using Pharos, and the previously performed GreenScreen® by ToxServices (2015) has expired. Therefore, a full GreenScreen® is required.
- Caprylyl glycol is not listed on the U.S. DOT list .
- Caprylyl glycol is on the following list for multiple endpoints:
    - German FEA – Substances Hazardous to Waters – Class 1 – Low Hazard to Waters
- Caprylyl glycol is not present on any GreenScreen®-specified lists for single.

Hazard Statement and Occupational Control

The Globally Harmonized System of Classification and Labelling of Chemicals (GHS) hazard statements identified for caprylyl glycol self-assigned in its European Chemicals Agency (ECHA) registration dossier 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 Caprylyl Glycol (CAS #1117-86-8) (ECHA, CAS #1117-86-8, 2024)

H Statement	H Statement Details
H319	Causes serious eye irritation (GHS Category 2)

Table 2: Occupational Exposure Limits and Recommended Personal Protective Equipment for Caprylyl Glycol (CAS #1117-86-8)

Personal Protective Equipment (PPE)	Reference	Occupational Exposure Limits (OEL)	Reference
Avoid contact with skin, eyes (tightly fitting safety goggles (splash goggles)), and clothes.	ECHA, CAS #1117-86-8, 2024	None	Not applicable

Physicochemical Properties of Caprylyl Glycol

Caprylyl glycol is a colorless liquid that is soluble in water. Its vapor pressure of 0.28 Pa indicates that it can form a vapor. Its measured log K_{ow} of 2.1 indicates a low potential for bioaccumulation.

Table 3: Physical and Chemical Properties of Caprylyl Glycol (CAS #1117-86-8)

Property	Value	Reference
Molecular formula	$C_8H_{18}O_2$	PubChem 2024
SMILES Notation	CCCCCCC(CO)O	PubChem 2024
Molecular weight	146.23 g/mol	PubChem 2024
Physical state	Liquid	CIR 2012, ECHA, CAS #1117-86-8, 2024
Appearance	Almost colorless liquid	CIR 2012, ECHA, CAS #1117-86-8, 2024
Melting point	28-31°C (OECD Test Guideline (TG) 102 and EU Method A.1)	ECHA, CAS #1117-86-8, 2024
Boiling point	267°C (OECD TG 103 and EU Method A.2)	ECHA, CAS #1117-86-8, 2024
Vapor pressure	0.28 Pa at 25°C (OECD TG 104 and EU Method A.4)	ECHA, CAS #1117-86-8, 2024

Table 3: Physical and Chemical Properties of Caprylyl Glycol (CAS #1117-86-8)		
Property	**Value**	**Reference**
Water solubility	7.5 g/L at 20°C (OECD TG 105 and EU Method A.6)	ECHA, CAS #1117-86-8, 2024
Dissociation constant	Not identified	
Density/specific gravity	0.93 g/cm³ at 20°C (OECD TG 109 and EU Method A.3)	ECHA, CAS #1117-86-8, 2024
Partition coefficient	Log K_{ow} = 2.1 at 25°C and pH of 6 (OECD TG 117 and EU Method A.8)	ECHA, CAS #1117-86-8, 2024

Toxicokinetics

Limited *in vitro* data using pig skin suggest that caprylyl glycol penetrates the skin and undergoes metabolism within the dermis/epidermis, and the unchanged compound was not detected in the receptor fluid (Beiersdorf 2010, as cited in CIR 2012). The Personal Care Products Council predicted dermal penetration of caprylyl glycol would be about 80% based on modeling (PCPC 2010, as cited in CIR 2012).

In the absence of measured metabolic data for the oral route of exposure for 1,2-glycols, CIR (2012) evaluated the C6-12 1,2-glycols, including caprylyl glycol, using structural features, a substructure search, and modeling (Meteor 9.0). CIR predicted the compounds would likely be metabolized by *C*-oxidation, *C*-hydroxylation, glucuronidation, and β-oxidation (CIR 2012). The prediction corresponds with measured data for shorter-chained (C4) surrogate 1,2-butanediol, which, following intravenous administration in rabbits, was excreted in the urine as the glucuronide conjugate, and unchanged, and there was no observed accumulation in the tissues (CIR 2012).

No further data were found characterizing the absorption, distribution, metabolism, or excretion of caprylyl glycol for the dermal, oral, or inhalation routes of exposure.

Hazard Classification Summary

Group I Human Health Effects (Group I Human)

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

Caprylyl glycol was assigned a score of Low for carcinogenicity based on surrogate data and modeling. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when adequate negative data are available and they are not GHS classified (CPA 2018b). Confidence in the score is high based on reliable data for a conservative surrogate, supported by 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.
- UNEP 2001, ECHA, CAS #57-55-6, 2024, CIR 2012
  - *Oral: Surrogate: Propylene glycol (CAS #57-55-6):* A non-GLP compliant 2-year chronic toxicity/carcinogenicity study (guideline not reported) was conducted using male and female Crj: CD(SD) rats (30/sex/dose group). Rats were provided diets containing propylene glycol (purity not specified) at 0, 6,250, 12,500, 25,000, or 50,000 ppm (reported to be equivalent to 0, 200, 400, 900, and 1,700 mg/kg/day for males and 0, 300, 500, 1,000, and 2,100 mg/kg/day for females, respectively) for 2 years. No evidence of treatment-related tumor

induction was observed with treatment (Klimisch 2, reliable with restrictions) (Gaunt et al. 1972).

- *Oral:* *Surrogate: Propylene glycol (CAS #57-55-6):* A non-GLP compliant 2-year chronic toxicity/carcinogenicity study (guideline not reported) was conducted using male and female rats (strain not specified). Animals were exposed via drinking water at 0, 1, 2, 5, 10, 25, and 50% (reported to be equivalent to 0, 1,600, 3,680, 7,700, 13,200, 21,000, and 37,000 mg/kg/day) for 140 days (5/sex/dose). Animals were evaluated based on food and water consumption, body weights, urinalysis, gross pathology, and histopathology of the kidneys, heart, spleen, and liver. All animals exposed at ≥ 25% died within the first 9 days of exposure. Food intake was slightly reduced in the 10% group compared to controls; however, there were no significant effects on water consumption or body weights in groups exposed at up to 10%. Albuminuria, cells, or casts in the urine were identified in animals administered 1 to 10% solutions (no further details provided). There were no significant findings based on gross pathology or histopathology in rats exposed at up to 10%. The NOAEL was assigned at 13,200 mg/kg/day (Klimisch 2, reliable with restrictions) (Seidenfeld and Hanzlik 1932).
- *Oral:* *Surrogate: Propylene glycol (CAS #57-55-6):* Albino rats were provided diets containing propylene glycol (purity not specified) at 0, 2.45 and 4.9% in the diet for 2 years (6 males and 4 females/dose). Animals were evaluated based on cage side observations, food and water consumption, body weights, food efficiency, gross pathology, and histopathology of the lung, heart, liver, kidney, adrenal, and testis (routinely), and the pancreas, stomach, intestines, and lymph in about half of the animals, and other organs occasionally. Slight chronic liver damage was the only effect reported (no further details provided). The NOAEL was assigned at 4.9% in the diet (Klimisch 2, reliable with restrictions) (Morris et al. 1941).
- *Oral:* *Surrogate: Propylene glycol (CAS #57-55-6):* A non-GLP compliant 2-year chronic toxicity/carcinogenicity study (method not reported) was conducted using male and female Beagle dogs (5/sex/dose group). Dogs were provided food containing propylene glycol (USP) at 0, 8%, or 20% (equivalent to 0, 2,000, and 5,000 mg/kg/day, respectively) for 2 years. Tumor incidences were unchanged in male and female dogs when compared to the controls (Klimisch 2, reliable with restrictions) (Weil et al. 1971).
- *Dermal:* *Surrogate: Propylene glycol (CAS #57-55-6):* In a skin painting study, propylene glycol was administered to female mice at 2, 10 or 21 mg/day over the lifetime. No increase in dermal tumors was observed (Klimisch 2, reliable with restrictions) (Stenbäck and Shubik 1974).
- *Inhalation:* *Surrogate: Propylene glycol (CAS #57-55-6):* Groups of 20 white rats were exposed to a supersaturated atmosphere with propylene glycol vapor (> 350 mg/m^3), whole-body, 24 hours/day, for up to 18 months. The number of rats was increased by birth of young. Observations in life were recorded for body weight gain, coat color, conjunctival effects, number of young born, and general conditions. Rats were sacrificed at intervals of 3 to 18 months from the beginning of exposure. Urine was aspirated from the bladder for urinalysis, gross pathological and histopathological (lungs, liver, kidney, and spleen) examinations were performed. There were no increases in tumor incidence observed (Klimisch 2, reliable with restrictions) (Robertson et al. 1947).
- *Inhalation:* *Surrogate: Propylene glycol (CAS #57-55-6):* Two groups of Macaca Rhesus monkeys were exposed to propylene glycol vapor at 100 to 220 mg/m^3 (about 60% saturation), and > 350 mg/m^3 (supersaturation), whole-body, 24 hours/day, for 1 to 13 months (14-15 animals/sex/ group, and 16/sex in the control group). Animals were evaluated based on body weight changes, texture and color of hair and skin, condition of

eyes, appetite, activity, and any abnormal signs or symptoms. Complete blood counts were performed at the beginning of the experiment, and again just prior to sacrifice. Tests for the ability of the kidneys to concentrate urine were conducted at the end of the observation period. Gross pathology and microscopic examinations of the liver, kidneys, spleen, mesenteric glands, adrenals and in certain cases stomach, intestines and tested were performed. Infections with parasitic nematodes and lung mites were found in almost all of the animals. There were no increases in tumor incidence observed (Klimisch 2, reliable with restrictions) (Robertson et al. 1947).

- Toxtree 2018
  - Toxtree modeling predicted caprylyl glycol would be negative for both genotoxic and non-genotoxic carcinogenicity using the ISS model (see Appendix D).
- VEGA 2023
  - Carcinogenicity modeling of caprylyl glycol was performed using the VEGA platform. If an external compound is beyond the defined scope of a given model, it is considered outside that model's applicability domain (AD) and cannot be associated with a reliable prediction (Sahigara 2007). Values for AD index (ADI) range from 0 (worst case) to 1 (best case). Generally, ADI values of > 0.70 indicate that the prediction has moderate or better predictivity (Gad 2016). Three of six models provided predictions which are considered moderately-to-highly reliable, and suggest caprylyl glycol will be non-carcinogenic. The remaining models had insufficient reliability and are therefore not included in the weight of evidence (VEGA 2023, Appendix E). Predictions are summarized as follows:
    - The CAESAR model predicted caprylyl would be **non-carcinogenic** with moderate reliability based on a global ADI value of **0.793**.
    - The ISS model predicted caprylyl would be non-carcinogenic with low reliability based on a global ADI value of 0.
    - The IRFMN-ISSCAN-CGX model predicted caprylyl would be non-carcinogenic with low reliability based on a global ADI value of 0.532.
    - The IRFMN-Antares model predicted caprylyl would be **non-carcinogenic** with high reliability based on a global ADI value of **0.933**.
    - The IRFMN oral classification model predicted caprylyl would be carcinogenic with low reliability based on a global ADI value of 0.
    - The IRFMN inhalation classification model predicted caprylyl would **be non-carcinogenic** with high reliability based on a global ADI value of **0.902**.
- DTU 2024
  - Danish (Q)SAR Database for the CAS number 1117-86-8 reports that caprylyl glycol is in the domains of six of the seven of the E Ultra FDA RCA cancer software systems and is predicted to be negative for carcinogenicity in all six databases (female rat, rat, male mouse, female mouse, mouse, and rodent). Caprylyl glycol is in the domain of two of the seven Leadscope FDA RCA cancer databases, and is predicted it to be negative for carcinogenicity in both databases (female rat, mouse). Regarding the liver specific cancer in rat or mouse model, caprylyl glycol is within the domain of the two models (CASE Ultra and Leadscope) and the overall battery, and is predicted to be negative in all three (Appendix F).
- U.S. EPA 2019, 2021
  - Attempts were made to evaluate the carcinogenic potential of caprylyl glycol using the most current version of OncoLogic (v9.0); however, OncoLogic indicated that its chemical class is not supported in the current version of software. Since the knowledge base used in this version of the program has not changed from the last version, ToxServices used the previous version (v8.0) to evaluate the carcinogenic potential of caprylyl glycol. ToxServices

evaluated this chemical as an aliphatic alcohol. Medium sized alcohols (C 6-20) are of carcinogenic concern when they can be oxidized to metabolically persistent carboxylic acids (e.g., ω – 1 branched fatty acids). As caprylyl glycol is not metabolically persistent, and was negative for genotoxicity in *in vitro* assays (see genotoxicity section below), it has a low concern for carcinogenicity (Appendix G).

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

Caprylyl glycol was assigned a score of Low for mutagenicity/genotoxicity based on negative results for mutagenicity and clastogenicity in *in vitro* assays. 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 low because there are some apparent deficiencies in the only *in vitro* chromosome aberration test, and also in the *in vitro* mammalian cell gene mutation test.

- 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 #1117-86-8, 2024
  - *In vitro* – Caprylyl glycol was not mutagenic in a GLP-compliant bacterial reverse mutation assay conducted according to OECD TG 471, EU Method B.13/14, and EPA OPPTS 870.5100, using the plate-incorporation and pre-incubation methods. *Salmonella typhimurium* tester strains TA 1535, TA 1537, TA 98 and TA 100 and *E. coli* WP_2 *uvr* A were exposed to caprylyl glycol (purity not specified) in DMSO at concentrations up to 5,000 µg/plate, with and without metabolic activation. No increase in the mutation frequency was observed in the presence or absence of metabolic activation in any strain, at any concentration, with or without activation. Cytotoxicity was observed in all strains at 5,000 µg/plate and in some strains at lower concentrations with and without activation (further details not reported). Positive and vehicle controls performed as expected. Authors conclude the test substance was not mutagenic under the conditions of the test (Klimisch 1, reliable without restrictions) (Unnamed 2008 study report).
  - *In vitro* – Caprylyl glycol was not mutagenic in a GLP-compliant bacterial reverse mutation assay conducted according to OECD Test TG 471, and EU Method B.13/14, using the pre-incubation method. *S. typhimurium* tester strains TA 1535, TA 1537, TA 98 and TA 100 and *E. coli* WP_2 *uvr* A were exposed to caprylyl glycol (purity not specified) in DMSO at concentrations up to 5,000 µg/plate, with and without metabolic activation (Experiment I), and at up to 5,000 µg/plate without activation (Experiment II). No increase in the mutation frequency was observed in the presence or absence of metabolic activation in any strain, at any tested concentration, with or without activation, including cytotoxic concentrations. Cytotoxicity was observed in TA 100 at ≥ 500 µg/plate without activation, and in *E. coli* at ≥ 1,500 µg/plate without activation. Positive and vehicle controls performed as expected. Authors conclude the test substance was not mutagenic under the conditions of the test (Klimisch 2, reliable with restrictions) (Unnamed 1999 study report).
- ECHA, CAS #1117-86-8, 2024, CIR 2012
  - *In vitro* – Caprylyl glycol was not mutagenic in a GLP-compliant mammalian cell gene mutation test conducted according to OECD TG 476 and EU Method B.17. Chinese hamster lung fibroblasts (V79) cells were exposed to caprylyl glycol (purity not specified) in dimethyl sulphoxide (DMSO) at concentrations up to 1,480 µg/mL, with and without metabolic activation for 4 hours (Experiment I), and at up to 1,480 µg/mL, without activation for 24 hours (Experiment II). No increase in the mutation frequency was

observed in the presence or absence of metabolic activation. Controls performed as expected. The highest concentrations were determined based on cytotoxicity based on relative cloning efficiency (further details not provided) (Klimisch 1, reliable without restrictions) (Unnamed 2009 study report). *It may be noted that ECHA (2022) discounted the reliability of this study based on reporting deficiencies (i.e., insufficient details on cytotoxicity, insufficient details on results for the positive control, insufficient information on the negative control, and lack of reported numerical data for the cytotoxicity and mutation frequencies observed).*

- *In vitro* – Caprylyl glycol was not clastogenic in a GLP-compliant chromosomal aberration test performed in a manner equivalent or similar to the Japanese Guideline on Genotoxicity Tests No. 1604, and OECD TG 473. Chinese hamster lung (CHL/IU) cell lines were exposed to caprylyl glycol in DMSO at concentrations up to 700 ug/mL, with and without metabolic activation for 6 hours (Experiment I), and up to 180 µg/mL with and without activation for 24 hours (Experiment II). The highest concentrations were based on cytotoxicity based on the IC50 (i.e., 50% growth inhibition). No increase in the frequency of chromosome aberrations was observed with treatment in the presence or absence of metabolic activation. Controls performed as expected (Klimisch 2, reliable with restrictions) (Unnamed 2007 study report). *It may be noted that ECHA (2022) discounted the reliability of this study based on reporting deficiencies that do not correspond with OECD TG 473 (i.e., reduced cell proliferation rates were not reported to correspond with cytotoxic concentrations, only 200 metaphases were scored instead of at least 300 required by the test guideline, there is insufficient reporting on the results for the positive control, and there is insufficient reporting of cytotoxicity and/or frequency of cells with structural chromosomal aberrations for the treated and control cultures).*

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

Caprylyl glycol was conservatively assigned a score of Low for reproductive toxicity based on a lack of treatment related reproductive toxicities in an OECD TG 421 reproductive/developmental toxicity screening test. GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when adequate data are available and negative (CPA 2018b). Confidence is low because the OECD TG 421 studies use a low number of animals, which inherently reduces statistical confidence.

- 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 #1117-86-8, 2024
  - *Oral:* Caprylyl glycol was evaluated in a GLP-compliant Reproductive / Developmental Toxicity Screening Test performed according to OECD TG 421. Wistar rats were administered the test substance (purity not specified) by gavage in polyethylene glycol (PEG 300) at 0, 150, 300, or 1,000 mg/kg/day (10/sex/dose). Males were exposed for 42 days beginning at 2 weeks prior to mating. Females were exposed for 40-45 days beginning at 2 weeks prior to mating and up through lactation day (LD) 4. Clinical observations included semi-solid feces in 2/10 males at 1,000 mg/kg/day from days 5 to 9. One high dose dam was found dead on day 37 (gestation day (GD) 21) due to dystocia (birthing difficulties such as large or awkwardly positioned fetus, small pelvis, and/or insufficient contractions), which investigators did not consider to be treatment-related. Decreased body weights were determined in males and females at 1,000 mg/kg/day (severity not specified). There were no significant findings based on food consumption, histopathology (limited to the reproductive organs), sperm measures, or reproductive performance. In pups, the day 4 survival index

was significantly lower at 300 and 1,000 mg/kg/day compared to concurrent controls; however, it was reported to be due to a complete litter loss from a single dam at 300 mg/kg/day, and litter losses in 2 dams at 1,000 mg/kg/day during the lactation period. As a similar incidence of total litter loss was spontaneously observed in a previous OECD 421 study in the same laboratory (no further details provided), investigators considered it unrelated to treatment. The NOAEL for systemic toxicity was assigned at 300 mg/kg/day, based on decreased body weights at 1,000 mg/kg/day in both sexes. The NOAEL for reproductive and developmental toxicity was assigned at 1,000 mg/kg/day, the highest dose tested (Klimisch 1, reliable without restrictions) (Unnamed 2013 study report).

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M, or L): *M*
Caprylyl glycol was conservatively assigned a score of Moderate for developmental toxicity based on dose-related total litter loss during the lactation period in rats in a Reproductive / Developmental Toxicity Screening Test (OECD TG 421). Study details are insufficient to determine if the litter loss was secondary to maternal toxicity or effects on or via lactation, and therefore meet the criteria for GHS Category 2 classification. In addition, decreased fetus body weight was reported in a prenatal developmental toxicity study in rats in the presence of maternal toxicity, also supporting GHS Category 2. GreenScreen® criteria classify chemicals as a Moderate hazard for reproductive toxicity when data meet the criteria for GHS Category 2 (CPA 2018b). Confidence is low because the OECD TG 421 studies use a low number of animals, which inherently reduces statistical confidence, and as noted, there are insufficient data to determine if the developmental effects in the OECD TG 421 and OECD TG 414 studies were secondary to maternal toxicity.

- 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 #1117-86-8, 2024
  - *Oral:* Caprylyl glycol was evaluated in a GLP-compliant Prenatal Developmental Toxicity Study performed according to OECD TG 414. Pregnant Wistar rats were administered the test substance (purity not specified) by gavage in polyethylene glycol (PEG 300) at 0, 150, 300, or 1,000 mg/kg/day (24/dose) on GD 5 to 19. The dams were sacrificed and caesarian sections were performed on GD 20. There were no significant findings based on clinical signs of toxicity, mortality, food consumption, or gross pathology. The mean body weight gain was statistically significantly increased at all dose levels compared to controls, which is not considered an adverse effect. There were no significant findings based on number of abortions, pre- and post-implantation loss, total litter loss by resorption, early or late resorptions, number of dead fetuses, pregnancy duration, or the number of pregnant dams. Mean fetus weights were significantly lower at all dose levels compared to concurrent controls (severity not specified); however, the results were only significantly different compared to historical controls at 1,000 mg/kg/day. There was a significantly increased incidence of a 14th accessory rib in fetuses at 1,000 mg/kg/day, which is reported as a sign of fetotoxicity due to the significant reduction of fetal weights at the same dose level. The NOAEL for maternal toxicity was assigned at 150 mg/kg/day, based on lower uterine gravid weight at ≥ 300 mg/kg/day. The NOAEL for developmental toxicity was assigned at 300 mg/kg/day based on decreased fetus body weights and increased incidence of supernumerary ribs at 1,000 mg/kg/day. The NOAEL for teratogenicity was assigned at 1,000 mg/kg/day (Klimisch 1, reliable without restrictions) (Unnamed 2013 study report). *ToxServices assigned a NOAEL of 300, and LOAEL of 1,000 mg/kg/day based on decreased fetus body weights. ToxServices did not consider the increased incidence of a 14th rib to be*

toxicologically significant as supernumerary ribs are common and not developmentally important. Furthermore, the severity of decreased fetus body weights was not reported. In the absence of additional data, ToxServices assigned ***GHS Category 2*** *classification on the conservative assumption that the magnitude of fetus body weight decreases was not secondary to maternal toxicity, and was greater than 5%, and therefore toxicologically relevant.*

- *Oral:* As summarized previously, caprylyl glycol was evaluated in a GLP-compliant Reproductive / Developmental Toxicity Screening Test performed according to OECD TG 421. Wistar rats were administered the test substance (purity not specified) by gavage in polyethylene glycol (PEG 300) at 0, 150, 300, or 1,000 mg/kg/day (10/sex/dose). Males were exposed for 42 days beginning at 2 weeks prior to mating. Females were exposed for 40-45 days beginning at 2 weeks prior to mating and up through LD 4. Clinical observations included semi-solid feces in 2/10 males at 1,000 mg/kg/day from days 5 to 9. One high dose dam was found dead on day 37 (GD 21) due to dystocia (birthing difficulties such as large or awkwardly positioned fetus, small pelvis, and/or insufficient contractions), which investigators did not consider to be treatment-related. Decreased body weights were determined in males and females at 1,000 mg/kg/day (severity not specified). There were no significant findings based on food consumption, histopathology (limited to the reproductive organs), sperm measures, or reproductive performance. In pups, the day 4 survival index was significantly lower at 300 and 1,000 mg/kg/day compared to concurrent controls; however, it was reported to be due to a complete litter loss from a single dam at 300 mg/kg/day, and litter losses in 2 dams at 1,000 mg/kg/day during the lactation period. As a similar incidence of total litter loss was spontaneously observed in a previous OECD TG 421 study in the same laboratory (no further details provided), investigators considered it unrelated to treatment. The NOAEL for systemic toxicity was assigned at 300 mg/kg/day, based on decreased body weights at 1,000 mg/kg/day in both sexes. The NOAEL for reproductive and developmental toxicity was assigned at 1,000 mg/kg/day, the highest dose tested (Klimisch 1, reliable without restrictions) (Unnamed 2013 study report). *ToxServices does not agree that the apparent dose-related litter losses (i.e., litter loss in one dam at 300 mg/kg/day, and litter loss in two dams at 1,000 mg/kg/day) were sufficiently addressed. While screening studies have inherent statistical limitations based on the low number of animals/group, it would be appropriate to compare the litter losses to historical controls over numerous studies, and not just one study. Accordingly, ToxServices assigned* ***GHS Category 2*** *based on litter loss being questionably relevant at 300 and at 1,000 mg/kg/day, in the presence of decreased body weights of the parental animals at 1,000 mg/kg/day, and altogether the data are insufficient to determine if the litter losses are more than spurious, and/or if they are secondary to maternal toxicity or effects on or via lactation.*

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

Caprylyl glycol was assigned a score of Data Gap for endocrine activity based on lack of sufficient data. While modeling and *in vitro* high throughput screening assays were negative for estrogen, androgen, thyroid, and steroidogenesis pathways, and no specific adverse effects plausibly related to endocrine activity were identified in any of the toxicity studies identified herein, no *in vivo* studies focusing on endocrine activity as an explicit endpoint were identified.

- 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 2024b

- Caprylyl glycol was inactive in 6/6 estrogen receptor (ER) assays, 6/6 androgen receptor (AR) assays, 1/1 steroidogenesis assays, and 10/10 thyroid receptor assays performed as part of the U.S. EPA's Endocrine Disruptor Screening Program (EDSP) in the 21st Century (Appendix H).
- Caprylyl glycol was predicted to be inactive for estrogen receptor agonism, antagonism, and binding by the ToxCast CERAPP Potency Level (From Literature) model (Appendix I).

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

Caprylyl glycol was assigned a score of Low for acute toxicity based on oral LD_{50} values > 2,000 mg/kg in two studies with the target compound, and a 4-hour inhalation LC_{50} > 7.015 mg/L for the surrogate pentane-1,2-diol. GreenScreen® criteria classify chemicals as a Low hazard for acute toxicity when oral and dermal LD_{50} values are > 2,000 mg/kg, and inhalation LC_{50} values are > 5 mg/L (mist) (CPA 2018b). Although no dermal data were found, dermal data are not required. Furthermore, dermal LD_{50} values are typically higher than oral values based on decreased absorption through the skin. The confidence in the score is high based on measured data for the target compound 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 #1117-86-8, 2024
  - *Oral:* In a GLP-compliant acute toxicity study conducted according to OECD TG 401 and EU Method B.1, Sprague-Dawley rats (5/sex/dose) were administered caprylyl glycol (purity not specified) at a single dose of 2,000 mg/kg by gavage in arachis oil BP. Animals were observed for 14 days post-administration. No mortalities or treatment-related effects on body weight were reported. The oral LD_{50} was > 2,000 mg/kg (Klimisch 2, reliable with restrictions) (Unnamed 1999 study report).
  - *Inhalation*: *Surrogate: Pentane-1,2-diol:* In an acute inhalation toxicity study with a protocol similar to the OECD TG 403, Tif:RAI f (SPF) rats (10/sex/dose) were exposed to the test substance (purity not specified) as aerosol (no vehicle), nose-only, at nominal concentrations of 0, 96.7, and 290.0 mg/L (0, 3.380, and 7.015 mg/L measured, respectively) for 4 hours. Animals were observed for 14 days post-exposure. No mortalities were observed. The 4-hour LC_{50} was > 7.015 mg/L (Klimisch 2, reliable with restrictions) (Unnamed 1982 study report).
- CIR 2012
  - *Oral:* In an acute oral toxicity study with limited details, male and female rats (number and strain not stated) were exposed orally to caprylyl glycol. Deaths occurred within 2 h after administration. The LD_{50} was 2,240 mg/kg in males, and 2,200 mg/kg in females.

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

Caprylyl glycol was assigned a score of Low for systemic toxicity (single dose) based on lack of indications of systemic toxicity at sublethal doses in two acute oral exposure studies with the target substance, and one acute inhalation study with the surrogate pentane-1,2-diol. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (single dose) when adequate data exist for at

least one route of exposure, and GHS classification is not warranted (CPA 2018b). The confidence in the score is high based on measured data for the target compound 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 #1117-86-8, 2024
    - *Oral:* As summarized previously, caprylyl glycol was evaluated in a GLP-compliant acute toxicity study conducted according to OECD TG 401 and EU Method B.1. Sprague-Dawley rats (5/sex/dose) were administered caprylyl glycol (purity not specified) at a single dose of 2,000 mg/kg by gavage in arachis oil BP. Animals were observed for 14 days post-administration. No mortalities or treatment-related effects on body weight were reported. Clinical signs of toxicity were seen in all animals on the first day of dosing (Day 0) including hunched posture, lethargy, ataxia, decreased respiratory rate, and labored respiration, and none of these effects were observed on day 2 or thereafter (Klimisch 2, reliable with restrictions) (Unnamed 1999 study report). *ToxServices considered the clinical signs indicative of transient narcotic effects that are assessed separately under single exposure neurotoxicity section, and identified the NOAEL at 2,000 mg/kg/day based on the lack of indications of systemic toxicity.*
    - *Inhalation*: *Surrogate: Pentane-1,2-diol:* As summarized previously, pentane-1,2-diol was evaluated in an acute inhalation toxicity study with a protocol similar to OECD TG 403. Tif:RAI f (SPF) rats (10/sex/dose) were exposed to the test substance (purity not specified) as aerosol (no vehicle), nose-only, at nominal concentrations of 0, 96.7, and 290.0 mg/L (0, 3.380, and 7.015 mg/L measured, respectively) for 4 hours. Animals were observed for 14 days post-exposure. No mortalities were observed. Clinical signs of toxicity in both dose groups included ruffled fur and curved body position on the day of exposure; however, the effects were transient and no longer evident by day 2. Macroscopic examination revealed mottled or reddish lungs in a number of treated animals, but the incidence of these findings was not dose-related (Klimisch 2, reliable with restrictions) (Unnamed 1982 study report). *ToxServices identified the NOAEC at 7.015 mg/L/4h for this study based on the lack of significant systemic toxicity.*
- CIR 2012
    - *Oral:* As summarized previously, caprylyl glycol was evaluated in an acute oral toxicity study reported with limited details. Male and female rats (number and strain not stated) were exposed orally to caprylyl glycol. Signs of toxicity were seen at doses ≥ 464 mg/kg and theses included sedation and ataxia. Loss of muscle tone and dyspnea were observed at 1,000 mg/kg, and lateral position, coma, and death were observed at a dose of 1,470 mg/kg. Deaths occurred within 2 h after administration. Surviving animals recovered within 24 hours. At necropsy, pale parenchymal organs were observed in 3,160 and 4,640 mg/kg dose groups. Study authors identified the NOAEL of 215 mg/kg in this study. *ToxServices considered the sedation, ataxia, and loss of muscle tone to be indicative of transient narcotic effects and assessed them separately in the single exposure neurotoxicity section. As this was an oral exposure study, the dyspnea is unlikely due to respiratory tract irritation, but may be related to the loss of muscle tone and/or other narcotic effects. Nevertheless, as surviving animals recovered within 24 hours, ToxServices did not consider any of the sublethal effects to be indicative of specific target organ (systemic) toxicity.*

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

Caprylyl glycol was assigned a score of Low for systemic toxicity (repeated dose) based on two oral exposure studies in rats for which the LOAEL values exceed the GHS guidance values (i.e., 100 mg/kg/day for 90-day studies and 300 mg/kg/day for 28-day studies); therefore, classification is not warranted. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (repeated dose) when adequate data exist for at least one route of exposure, and GHS classification is not warranted (CPA 2018b). The confidence in the score is high based on measured data for the target compound.

- 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 #1117-86-8, 2024
  - *Oral*: Caprylyl glycol was evaluated in a GLP-compliant Repeated Dose 90-day Toxicity Study in Rodents performed according to OECD TG 408. Wistar rats were exposed to the test substance (purity not specified) by gavage in PEG 300 at 0, 150, 300, or 1,000 mg/kg/day (10/sex/dose) for 90 days. Semi-solid feces was observed for 8/10 males at 1,000 mg/kg/day on a few occasions in the first week only, and there were no further significant findings based on clinical observations. There were no significant increases in mortality in treated animals compared to controls. Decreased body weights and weight gains were measured in several weeks in both sexes at ≥ 300 mg/kg/day (severity not specified), and corresponded with decreased food consumption at 1,000 mg/kg/day. Although food efficiency was not determined in the study, authors of the REACH dossier reported a clear reduction in food efficiency with increasing dose. There were no significant findings based on ophthalmology, hematology, clinical chemistry, urinalysis, gross pathology, or histopathology. The NOAEL was assigned at 150 mg/kg/day, and LOAEL at 300 mg/kg/day, based on decreased body weight and weight gain (Klimisch 1, reliable without restrictions) (Unnamed 2013 study report). *ToxServices notes that the LOAEL of 300 mg/kg/day exceeds the GHS Category 2 guidance value of 100 mg/kg/day; therefore, classification is not warranted.*
- ECHA, CAS #1117-86-8, 2024, CIR 2012
  - *Oral:* In a GLP-compliant repeated dose toxicity study conducted according to OECD TG 407 and EU Method B.7, Wistar rats (5/sex/dose) were administered daily doses of caprylyl glycol (purity not specified) by gavage in PEG 300 at doses of 0, 50, 300 or 1,000 mg/kg/day, 7 days/week, for 28 days. The animals were evaluated for clinical signs of toxicity, body weight, food consumption, hematology, clinical chemistry, gross pathology, and histopathology. No mortalities or treatment-related effects on clinical signs of toxicity, body weight, or food consumption were noted. Similarly, there were no treatment-related effects on hematology and clinical chemistry parameters. At 1,000 mg/kg/day there were increased absolute and relative kidney weights (males and females) and increased absolute and relative liver weights (males) (severities not specified); however, there were no corresponding histopathological findings. Minimal focal erosion at the limiting ridge was observed in 1 female at 1,000 mg/kg/day. Epithelial hyperplasia in the pars non-glandularis of the stomach was observed in 1 male at 300 mg/kg/day (minimal in severity), and in 1 male and 2 females at 1,000 mg/kg/day (minimal-to-slight in severity). Minimal hyperkeratosis in the pars non-glandularis was observed in 1 control female, 1 male at 300 mg/kg/day, and 4 males and 2 females at 1,000 mg/kg/day. Investigators attributed the stomach hyperplasia and hyperkeratosis in one animal at 300 and multiple animals at 1,000

mg/kg/day to local irritation, and assigned the NOEL at 50 mg/kg/day. The NOAEL for systemic toxicity was assigned at 300 mg/kg/day, and LOAEL at 1,000 mg/kg/day, based on elevated kidney weights at 1,000 mg/kg/day (Klimisch 1 (Unnamed 2004 study report). *The LOAEL of 1,000 mg/kg/day is above the GHS duration-adjusted guidance value of 300mg/kg/day for 28-day studies (the guidance value for a 90-day study is tripled for comparison to a 28-day study because 90/28 is approximately 3); therefore GHS classification is not warranted.*

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

Caprylyl glycol was assigned a score of Moderate for neurotoxicity (single dose) based on observations of transient narcotic effects in two acute oral toxicity studies with the target compound, and one acute inhalation toxicity study with the surrogate pentane-1,2-diol. Transient narcotic effects correspond with a GHS Category 3 classification . GreenScreen® criteria classify chemicals as a Moderate hazard for neurotoxicity (single dose) when data support GHS Category 3 classification (CPA 2018b). The confidence in the score is high based on measured data for the target compound 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.
- 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 #1117-86-8, 2024
  - *Oral:* As summarized previously, caprylyl glycol was evaluated in a GLP-compliant acute toxicity study conducted according to OECD TG 401 and EU Method B.1. Sprague-Dawley rats (5/sex/dose) were administered caprylyl glycol (purity not specified) at a single dose of 2,000 mg/kg by gavage in arachis oil BP. Animals were observed for 14 days post-administration. Clinical signs of toxicity were seen in all animals on the first day of dosing (Day 0) including hunched posture, lethargy, ataxia, decreased respiratory rate, and labored respiration, and none of these effects were observed on day 2 or thereafter (Klimisch 2, reliable with restrictions) (Unnamed 1999 study report). *ToxServices considered the clinical signs indicative of transient narcotic effects and identified the LOAEL at 2,000 mg/kg/day. Transient narcotic effects align with GHS Category 3 classification.*
  - *Inhalation*: <u>*Surrogate: Pentane-1,2-diol:*</u> As summarized previously, pentane-1,2-diol was evaluated in an acute inhalation toxicity study with a protocol similar to the OECD TG 403 guideline. Tif:RAI f (SPF) rats (10/sex/dose) were exposed to the test substance (purity not specified) as aerosol (no vehicle), nose-only, at nominal concentrations of 0, 96.7, and 290.0 mg/L (0, 3.380, and 7.015 mg/L measured, respectively) for 4 hours. Animals were observed for 14 days post-exposure. Clinical signs of toxicity in both dose groups included ruffled fur and curved body position on the day of exposure; however, the effects were transient and no longer evident by day 2 (Klimisch 2, reliable with restrictions) (Unnamed 1982 study report). *ToxServices notes that ruffled fur and curved body position may be indicative of general malaise and/or transient narcotic effects; therefore, GHS Category 3 classification is conservatively applied.*
- CIR 2012
  - *Oral:* As summarized previously, caprylyl glycol was evaluated in an acute oral toxicity study reported with limited details. Male and female rats (number and strain not stated) were exposed orally to caprylyl glycol. Signs of toxicity were seen at doses ≥ 464 mg/kg and theses included sedation and ataxia. Loss of muscle tone and dyspnea were observed

specifically at a dose of 1,000 mg/kg, and lateral position, coma, and death were observed at a dose of 1,470 mg/kg. Deaths occurred within 2 h after administration. At necropsy, pale parenchymal organs were observed in 3,160 and 4,640 mg/kg dose groups. Surviving animals recovered within 24 h, and study authors identified the NOAEL of 215 mg/kg in this study. *ToxServices considered sedation and ataxia as signs of transient narcotic toxicity, and assigned GHS Category 3 classification.*

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

Caprylyl glycol was assigned a score of Low for neurotoxicity (repeated dose) based on two oral repeated dose toxicity studies (90-day and 28-day) in which the lowest LOAEL identified was 1,000 mg/kg/day, based on reduced locomotor activity. A LOAEL of 1,000 mg/kg/day exceeds the GHS Category 2 guidance values of 100 mg/kg/day for 90-day studies and 300 mg/kg/day for 28-day studies; therefore classification is not warranted. GreenScreen® criteria classify chemicals as a Low hazard for neurotoxicity (repeated dose) when adequate data exist and GHS classification is not warranted (CPA 2018b). The confidence in the score is high based on measured data for the target compound.

- 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 #1117-86-8, 2024
  - *Oral:* As summarized previously, caprylyl glycol was evaluated in a GLP-compliant Repeated Dose 90-day Toxicity Study in Rodents performed according to OECD TG 408. Wistar rats were exposed to the test substance (purity not specified) by gavage in PEG 300 at 0, 150, 300, or 1,000 mg/kg/day (10/sex/dose) for 90 days. There were no significant findings based on clinical observations or gross pathology related to the nervous system, and no significant findings based on behavioral analyses including a functional observation battery (FOB) with assessment of sensory reactivity, appearance, behavior, respiratory parameters, landing hindlimb foot splay, fore- and hindlimb grip strength, and locomotor activity (Klimisch 1, reliable without restrictions) (Unnamed 2013 study report). *ToxServices assigned a NOAEL of 1,000 mg/kg/day for neurotoxicity, the highest dose tested. This exceeds the GHS Category 2 guidance value of 100 mg/kg/day; therefore, GHS classification is not warranted.*
- ECHA, CAS #1117-86-8, 2024, CIR 2012
  - *Oral:* As summarized previously, a GLP-compliant repeated dose toxicity study was conducted according to OECD TG 407 and EU Method B.7. Wistar rats (5/sex/dose) were administered daily doses of caprylyl glycol (purity not specified) by gavage in PEG 300 at doses of 0, 50, 300 or 1,000 mg/kg/day, 7 days/week, for 28 days. The animals were evaluated for clinical signs of toxicity, gross pathology, and neurobehavioral including a FOB with assessment of sensory reactivity, grip strength and motor activity. There were no significant findings based on clinical signs of toxicity, or gross pathology related to the nervous system. Neurobehavioral examination showed slightly reduced locomotor activity in males and females at 1,000 mg/kg/day (Klimisch 1, reliable without restrictions) (Unnamed 2004 study report). *ToxServices assigned a LOAEL for neurotoxicity at 1,000 mg/kg/day based on reduced locomotor activity. As this is above the GHS duration-adjusted guidance value of 300mg/kg/day for a 28-day study, GHS classification is not warranted.*

Skin Sensitization (SnS) (Group II*) Score (H, M, or L): L

Caprylyl glycol was assigned a score of Low for skin sensitization based on measured data. Caprylyl glycol was not sensitizing in a mouse local lymph node assay (LLNA) with exposures up to 25%

concentration, in a guinea pig maximization test (GPMT) with up to 75% concentration with an adjuvant, and up to 15% concentration in human repeat insult patch tests (HRIPTs). GreenScreen® criteria classify chemicals as a Low hazard for skin sensitization when adequate data exist and GHS classification is not warranted (CPA 2018b). Confidence is high based on reliable and consistent experimental data for 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 #1117-86-8, 2024
    - In a GLP-compliant mouse LLNA conducted according to OECD TG 429 guideline, female CBA mice (4/dose group) were dermally administered caprylyl glycol (purity not specified) at 5, 10, or 25% w/w in propylene glycol:water (7:3, v/v). The mice were administered 25 µL of the test substance to the dorsal surface of each ear for 3 consecutive days. Following the final application, the animals were sacrificed and the lymph nodes isolated to perform the proliferation assay. The stimulation indices for the 5, 10, and 25% doses were 1.4, 1.2 and 2.0, respectively. As all of the stimulation indices for the applied doses were less than 3, caprylyl glycol was not sensitizing to the skin of mice in this study (Klimisch 1, reliable without restrictions) (Unnamed 2003 study report).
    - Caprylyl glycol was evaluated in a GLP-compliant GPMT performed according to Japanese Guideline No. 24. Male Hartley guinea pigs (10 test animals and 5 controls) were induced with the test substance (purity not specified) via intradermal injection on day 1 with the test substance at 25 or 75% in olive oil, or at 25% + 50% Freund's Complete Adjuvant (FCA) in 25% olive oil. The second induction was performed on day 8 and the neat test substance was applied over the injection sites for 48 hours under occlusion at 0.2 mL. The challenge was applied on day 22 and the neat test substance was applied to freshly clipped and shaved flanks for 24 hours under occlusion at 0.1 mL. There were no indications of skin sensitization observed in any of the test animals at the 24 or 48 hour readings. Vehicle, adjuvant, and positive controls provided the expected results. Authors concluded that this substance was not sensitizing under the conditions of the test (Klimisch 2, reliable with restrictions) (Unnamed 2007 study report).
    - Caprylyl glycol (purity not specified) was evaluated in a GLP-compliant GPMT performed according to OECD TG 406. Dunkin-Hartley guinea pigs (10 test animals and 5 controls) were induced with the test substance (purity not specified) via intradermal injection on day 1 with the test substance at 50% solution in petrolatum, or at 25% + 25% sodium chloride + 25% FCA in 25% petrolatum. The second induction was performed on day 8 and the neat test substance was applied over the injection sites for 48 hours under semi-occlusion at 0.5 mL. The challenge was applied on day 25 and the test substance was applied to freshly clipped and shaved flanks for 24 hours under semi-occlusion as 0.25 mL of a 6.25% solution in 93.75% petrolatum (the maximum non-irritating concentration). There were no indications of skin sensitization observed in any of the test animals at the 1, 24, or 48 hours readings. Vehicle, adjuvant, and positive controls provided the expected results. Authors concluded that this substance was not sensitizing under the conditions of the test (Klimisch 2, reliable with restrictions) (Unnamed 1996 study report).
- CIR 2012
    - Caprylyl glycol (purity not specified) was not sensitizing in a maximization test conducted according to OECD TG 406 performed with 20 guinea pigs (sex and strain not specified). Animals were induced with 5% (in peanut oil) and 50% (in petrolatum) and challenged with 50% solution in petrolatum. No further details were provided.

  - Cosmetic formulations containing caprylyl glycol at concentrations up to 10% were not irritating or sensitizing in HRIPTs.
  - A preservative containing 15% 1,2-hexanediol and caprylyl glycol (50:50) in carbomer gel was not sensitizing, but caused irritation in 1 out of 205 participants in an HRIPT. A cosmetic formulation containing the same preservative at a concentration of 0.5% was not sensitizing in 224 volunteers.

Respiratory Sensitization (SnR) (Group II*) Score (H, M, or L): *L*

Caprylyl glycol was assigned a score of Low for respiratory sensitization based on lack of structural alerts for respiratory sensitization, combined with extrapolation from negative skin sensitization data. GreenScreen® criteria classify chemicals as a Low hazard for respiratory sensitization when adequate data exist and GHS classification is not warranted (CPA 2018b). Confidence in the score is low as this evaluation does not include assessment for 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 2023
  - Caprylyl glycol does not contain any structural alerts for respiratory sensitization (Appendix J).
- 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 caprylyl glycol 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 caprylyl glycol, and it does not contain any structural alerts for respiratory sensitization (OECD 2023, Appendix J), it is not expected to be a respiratory sensitizer.

Skin Irritation/Corrosivity (IrS) (Group II) Score (vH, H, M, or L): L

Caprylyl glycol was assigned a score of Low for skin irritation/corrosivity based on multiple animal studies in which the test substance was not irritating to the skin, even when tested up to full strength and the animals were exposed under occlusion. GreenScreen® criteria classify chemicals as a Low hazard for skin irritation/corrosivity when adequate data exist and GHS classification is not warranted (CPA 2018b). Confidence is high based on measured data for the target compound.

- 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 #1117-86-8, 2024
  - In a GLP-compliant dermal irritation test performed according to the Japanese Guide to Quasi-drug and Cosmetic Regulations (2006), three male New Zealand White rabbits were administered dermal applications of 0.5 mL undiluted caprylyl glycol (purity not specified) to clipped skin under occlusive dressing for 24 hours. Reactions were scored at 24, 48, and 72 hours after removal of the dressing. All scores for edema and erythema were zero at all

time points. Based on the results of this study, caprylyl glycol is not irritating to the rabbit skin (Klimisch 2, reliable with restrictions) (Unnamed 2007 study report).

- In another GLP-compliant dermal irritation test conducted according to EU Method B.4, three male New Zealand White rabbits were administered dermal applications of 0.5 mL undiluted caprylyl glycol (purity not specified) to clipped skin under occlusive dressing for 4 hours. Reactions were scored at 24, 48, and 72 hours after removal of the dressing. The mean erythema score at 24, 48, and 72h was 0.6/4 with effects being fully reversible within 48 hours. The mean edema score was 0. The study authors concluded that caprylyl glycol was not irritating to the skin in this study (Klimisch 1, reliable without restrictions) (Unnamed 2006 study report). *ToxServices notes that as neither the mean erythema nor mean edema scores were ≥ 1.5 in at least 2 of 3 tested animals, these results are below the threshold for GHS classification.*
- In a GLP-compliant 14-day repeated dose dermal toxicity study performed in accordance with a method published in the Official French Gazette (1982), six New Zealand White rabbits (sex not specified) were administered dermal applications of 0.5 mL of a 10% formulation of caprylyl glycol in Vaseline oil to shaved skin under semi-occlusive dressing for 24 hours. Reactions were scored at 24 and 72 hours after removal of the dressing. Very slight erythema (Grade 1, barely perceptible) was noted in 1 of 6 animals at 10% concentration. This finding had fully reversed (Grade 0) by 72 hours post treatment. The scores for edema were zero at every time point and the primary dermal irritation index (PDII) was 0.08/8. Therefore, caprylyl glycol was not irritating to the rabbit skin (Klimisch 2, reliable with restrictions) (Unnamed 1996 report). *ToxServices notes that this study was not performed according to the current dermal irritation OECD guideline, and therefore the scores reported are not directly comparable to the GHS criteria. However, the qualitative description did not support classification of caprylyl glycol under GHS.*
- In a GLP-compliant dermal irritation test (guideline not specified) Dunkin-Hartley guinea pigs (3/sex/dose) were administered daily caprylyl glycol dermally at concentrations of 6% and 3% v/v in liquid paraffin under non-occlusive conditions. An observation period of 14 days followed. Skin reactions (erythema and edema) were evaluated according to Draize method immediately before each daily application and at 24 hours after the final application. In addition, clinical signs of toxicity were recorded daily and bodyweights weekly. Treatment sites were re-shaved at appropriate intervals during the study. All scores for edema and erythema were zero at every time point. Based on the results of this study, caprylyl glycol is not irritating to the rabbit skin (Klimisch 2, reliable with restrictions) (Unnamed 1999 study report).

Eye Irritation/Corrosivity (IrE) (Group II) Score (vH, H, M, or L): H

Caprylyl glycol was assigned a score of High for eye irritation/corrosivity based on the results of a GLP-compliant Eye Irritation / Corrosion Test (EU Method B.5) in which the score for cornea opacity was > 1 in 2 of 2 animals, and the effects were fully reversible within 21 days, which aligns with GHS Category 2A criteria. GreenScreen® criteria classify chemicals as a High hazard for eye irritation/corrosivity when data support GHS Category 2A classification (CPA 2018b). The confidence in the score is high based on reliable measured 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 #1117-86-8, 2024

- In a GLP-compliant Eye Irritation / Corrosion Test conducted according to EU Method B.5, two male New Zealand White rabbits were administered 0.1 mL of undiluted caprylyl glycol (purity not specified) instilled into one eye each, with the contralateral eye serving as the control, and the eyes were rinsed with deionized water at 1 hour after application due to the conjunctival redness and chemosis which were grade 1 and 2, respectively. The eyes were scored at 48, 72, and 96 hours after instillation and the animals were observed for 14 to 16 days. At 24, 48, and 72 hours, the mean corneal score was 1.5/4 with the effects being fully reversible within 16 days; the mean iris score was 0.8/2 with the effects being fully reversible within 12 days; the mean conjunctival score was 1/3 with the effects being fully reversible within 11 days; and the mean chemosis score was 0.5/4 with effects being fully reversible within 7 days. Authors concluded the test substance was irritating to the eyes under the conditions of the test (Klimisch 1, reliable without restrictions) (Unnamed 2006 study report). *ToxServices notes this study meets the criteria for GHS Category 2A based on cornea opacity > 1 in at least 2 of 3 animals (or in this case 2 of 2 animals) and the effects were fully reversible within 21 days.*
- An Eye Irritation / Corrosion Test was performed according to the method specified in the Federal Register, Vol. 38, Iss. 187, p. 27019 (1973). Six New Zealand White rabbits (3/sex) administered ocular instillations of 0.1 g undiluted caprylyl glycol (purity not specified) into one eye each (rinsing not specified). The animals were evaluated at 1, 24, 48 and 72 hours and 7 days post-instillation. The mean corneal and iris scores were 0 and 0, respectively; the mean conjunctival score was 0.17/3 with the effects being fully reversible within 72 hours; and the mean chemosis score was 0.67/4 with effects being fully reversible within 72 hours. The study authors considered caprylyl glycol as not irritating to the rabbit eye under the conditions of the study (Klimisch 2, reliable with restrictions) (Unnamed 1979 study report). *ToxServices notes this study exceeds the criteria for GHS classification as none of the individual animal irritation scores exceeded 1 for corneal opacity or iritis, or 2 for conjunctival redness or edema, and all effects were fully reversible within 72 hours.*
- In another GLP-compliant ocular irritation study performed according to the method of the Official French Gazette (1992), three male New Zealand White rabbits were administered ocular instillations of 0.1 mL caprylyl glycol at 10% in Vaseline oil, in one eye each. The eyes were left unwashed after the application and animals were evaluated at 1, 24, 48, and 72 hours, and 4 and 5 days post-instillation. The mean corneal score was 0.3/4 with effects being fully reversible within 72 hours; the mean conjunctival score was 1.1/3 with the effects being fully reversible within 5 days; and the mean chemosis and iris scores were 0 and 0, respectively. Authors concluded the test substance was not irritating to the eyes under the conditions of the study (Klimisch 2, reliable with restrictions) (Unnamed 1996 study report). *ToxServices notes this study exceeds the criteria for GHS classification as none of the individual animal irritation scores exceeded 1 for corneal opacity or iritis, or 2 for conjunctival redness or edema, and all effects were fully reversible within 72 hours. It may be noted, however, that the test substance was only tested up to 10% concentration.*
- In another GLP-compliant ocular irritation test conducted according to OECD 405 and EU Method B.5, New Zealand White rabbits (1/dose; sex not specified) were administered ocular instillations of 0.1mL of 1%, 3%, and 5% v/v formulations of caprylyl glycol in liquid paraffin, into one eye each. The animals were evaluated at t 1, 24, 48, and 72 hours post-instillation. The mean scores for conjunctivae redness, iritis, cornea opacity and conjunctivae chemosis were all < 1 at 1, 3 and 5% concentrations with effects being fully reversible within 72 hours. This indicates that the substance is not an irritant to the rabbit eye. However, the study was considered inadequate for classification purpose of neat caprylyl glycol as only 1, 3 and 5% test material dilutions were tested with one animal each

(Klimisch 2, reliable with restrictions) (Unnamed 1998 study report). *ToxServices notes this study exceeds the criteria for GHS classification as none of the individual animal irritation scores exceeded 1 for corneal opacity or iritis, or 2 for conjunctival redness or edema, and all effects were fully reversible within 72 hours. It may be noted, however, that the test substance was only tested up to 5% concentration.*

- CIR 2012
  - In an *in vitro* HET-CAM assay (hen's egg test on the chorioallantoic membrane) for evaluating ocular irritation potential, caprylyl glycol was classified as a non-irritant at test concentrations of 1% and 3% in neutral oil. However, a mixture of 1,2-hexanediol and caprylyl glycol (50:50 (w/w)) was classified as a severe eye irritant in the HET-CAM assay at the concentration of 1% aqueous (effective concentration per ingredient = 0.5%). No further details were reported.

Ecotoxicity (Ecotox)

Acute Aquatic Toxicity (AA) Score (vH, H, M, or L): *M*

Caprylyl glycol was conservatively assigned a score of Moderate for acute aquatic toxicity based on a 96-hour LC_{50} of 14.1 mg/L in fish for the conservative surrogate 1,2-decanediol. This is supported by an unreliable study on the target chemical reporting a measured 96-hour LC_{50} of > 2.2 and ≤ 22 mg/L in fish. GreenScreen® criteria classify chemicals as a Moderate hazard for acute aquatic toxicity when the most sensitive trophic level has an L/EC_{50} value in the range of > 10 and < 100 mg/L (CPA 2018b). Confidence is low because, as noted by ECHA in its dossier evaluation, the available studies for all three trophic levels (fish, crustacea, and algae) have numerous deficiencies particularly regarding solubility limits, and the actual test substance concentrations to which each species were exposed. In addition, surrogate 1,2-decanediol is expected to be more aquatically toxic than 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.
- *Fish*
  - ECHA, CAS #1117-86-8, 2024
    - Caprylyl glycol was evaluated in a GLP-compliant Acute Toxicity Test performed according to OECD TG 203, with reduced number of fish (3/group instead of 7/group) because it was a range-finding study. *Danio rerio* (zebra fish) were exposed to the test substance (purity not specified) under static conditions for 96 hours at concentrations of 2.2, 22, 220, and 2,200 mg/L (nominal). Three of three fish died at 22 mg/L within 96 hours, and one of three died at 2.2 mg/L. Authors assigned the 96-hour LC_{50} at > 2.2 and ≤ 22 mg/L. Authors of the REACH dossier note that the test material was not stable in the relevant concentration range (Klimisch 2, reliable with restrictions) (Unnamed 1997 study report). *ECHA discounted the reliability of this study in its dossier evaluation (ECHA 2022) on the basis that less than 7 fish/group were exposed, which compromised statistical reliability, and because the study summary noted that the test substance was unstable in the medium and did not include details regarding measured concentrations or confirmation that the fish were exposed to the test substance below the critical micelle concentration (CMC).*
  - ECHA, CAS #5343-92-0, 2024
    - *Surrogate 1,2-Pentanediol (CAS #5343-92-0):* The test substance was evaluated in a GLP-compliant Acute Toxicity Test performed according to OECD TG 203. *D.*

rerio (zebra fish) were exposed to the test substance (> 99.0% purity) for 96 hours under static conditions at concentrations of up to 1,000 mg/L (nominal) (equivalent to maximum measured concentrations of 1,096.0 mg/L). There were no mortalities and the 96-hour LC_{50} was > 1,096 mg/L (measured) (Klimisch 1, reliable without restrictions) (Unnamed 1994 study report).

- ECHA, CAS #1119-86-4, 2024
  - *Surrogate 1,2-Decanediol (CAS #1119-86-4):* The test substance was evaluated in a GLP-compliant Acute Toxicity Test performed according to OECD TG 203 and EU Method C.1. *D. rerio* (zebra fish) were exposed to the test substance (purity not specified) for 96 hours under semi-static conditions at concentrations of 1.25, 2.50, 5.00, 10.0, and 20.0 mg/L (nominal). The measured concentrations were within 81-99% of the nominal concentrations at the start and the end of the exposure period. The 96-hour LC_{50} was **14.1 mg/L** (nominal) (Klimisch 1, reliable without restrictions) (Unnamed 2016 study report).

- *Crustacea*
  - ECHA, CAS #1117-86-8, 2024
    - Caprylyl glycol was evaluated in a GLP-compliant Acute Immobilization Test performed according to OECD TG 202 and ISO 6341. *Daphnia magna* were exposed to the test substance (purity not specified) at concentrations up to 1,000 mg/L (nominal) for 48 hours under semi-static conditions with renewal at 24 hours. The 48-hour EC_{50} was 176 mg/L (nominal) based on mobility (Klimisch 1, reliable without restrictions) (Unnamed 2007 study report). *ECHA discounted the reliability of this study in its dossier evaluation (ECHA 2022) on the basis that the test substance solubility was not adequately characterized and it was unclear if the daphnids were exposed to the test substance below the CMC.*
  - ECHA, CAS #5343-92-0, 2024
    - *Surrogate 1,2-Pentanediol (CAS #5343-92-0)*: The test substance was evaluated in a GLP-compliant Acute Immobilization Test performed according to OECD TG 202 and EU Method C.2. *D. magna* were exposed to the test substance (purity not specified) for 48 hours under static conditions at concentrations of up to 110 mg/L (nominal) (measured concentrations were within 93-94% of nominal at the start and end of the test period). There were no effects on mobility observed, and the 48-hour NOEC and EC_{50} were reported at 110 and > 110 mg/L, respectively (Klimisch 1, reliable without restrictions) (Unnamed 2012 study report).
  - ECHA, CAS #1119-86-4, 2024
    - *Surrogate 1,2-Decanediol (CAS #1119-86-4):* The test substance was evaluated in a GLP-compliant Acute Immobilization Test performed according to OECD TG 202 and EU Method C.2. *D. magna* were exposed to the test substance (purity not specified) for 48 hours under static conditions at concentrations up to 100 mg/L (nominal). The 48 hour EC_{50} was reported at **25.5 mg/L** (nominal) (Klimisch 1, reliable without restrictions) (Unnamed 2015 study report). *ToxServices notes test substance stability was not reported.*

- *Algae*
  - ECHA, CAS #1117-86-8, 2024
    - Caprylyl glycol was evaluated in a GLP-compliant Algal Growth Inhibition Test performed according to OECD TG 201 and ISO 8692. *Raphidocelis subcapitata* (green algae) were exposed to the test substance (purity not specified) at concentrations up to 200 mg/L (nominal) (measured concentrations were 76% of

nominal at test start (equivalent to 152 mg/L based on carbon content), and 81-86% of nominal at test end (equivalent to 167 mg/L based on carbon content of 110 mg/L based on TOC)) for 72 hours under static conditions. The 72-hour EC_{50} based on growth was 35 mg/L (measured) (Klimisch 1, reliable without restrictions) (Unnamed 2007 study report). *ECHA discounted the reliability of this study in its dossier evaluation (ECHA 2022) on the basis that the test substance solubility was not adequately characterized, testing appeared to have been performed well above the solubility limits, and it was unclear if the algae were exposed to the test substance at concentrations below the CMC.*

  - ECHA, CAS #5343-92-0, 2024
    - 72-hour growth rate EC_{50} (*Desmodesmus subspicatus*, green algae) = 9,334.69 mg/L (nominal) (non-GLP, DIN 38412 part 9) (Klimisch 2, reliable with restrictions) (Unnamed 1990 study report).
  - ECHA, CAS #1119-86-4, 2024
    - *Surrogate 1,2-Decanediol (CAS #1119-86-4):* The test substance was evaluated in a GLP-compliant Acute Immobilization Test performed according to OECD TG 201 and EU Method C.3. *R. subcapitata* (green algae) were exposed to the test substance (purity not specified) for 72 hours under static conditions at concentrations up to 100 mg/L (nominal), equivalent to 104 mg/L (measured in fresh and old medium). The 72-hour EC_{50} based on growth rate was **28.4 mg/L** (nominal) (Klimisch 1, reliable without restrictions) (Unnamed 2015 study report).

- Based on the weight of evidence, a score of Moderate was assigned. While a single study was available at each trophic level for caprylyl glycol, ECHA (2022) discounted those studies due to methodological deficiencies. In the absence of additional data, ToxServices examined available data for shorter and longer 1,2-alkane diols. The shorter alkyl chain would be expected to enhance biodegradability and water solubility, compared to the longer alkyl chain, and collectively, the aquatic toxicity of caprylyl glycol would be expected to fall within the range of toxicity for these two surrogates. Surrogate data suggest that the shorter chain surrogate 1,2-pentanediol is less toxic than the longer chain surrogate 1,2-decanediol, and therefore the longer chain surrogate is expected to be the most toxic among the three compounds. Surrogate 1,2-decanediol has acute L/EC_{50} values as low as 14.1 mg/L, supporting a Moderate score (10 – 100 mg/L).

Chronic Aquatic Toxicity (CA) Score (vH, H, M, or L): *M*

Caprylyl glycol was assigned a score of Moderate for chronic aquatic toxicity based on extrapolation from acute toxicity data. In accordance with the U.S. EPA Sustainable Futures guidance, the acute-to-chronic ratio (ACR) for estimating chronic toxicity of neutral organics is 10 for fish. Therefore, the above specified LC_{50} of > 2.2 and ≤ 22 mg/L for acute exposures, divided by the ACR of 10, is approximately 0.22 to 2.2 mg/L for caprylyl glycol, and for the conservative surrogate 1,2-decanediol a chronic value of 1.41 mg/L was derived. GreenScreen® criteria classify chemicals as a Moderate hazard for chronic aquatic toxicity when the most sensitive trophic level has a chronic toxicity value in the range of > 1 to 10 mg/L (CPA 2018b). Confidence is low because, as noted by ECHA in its dossier evaluation, the available studies for all three trophic levels (fish, crustacea, and algae) have numerous deficiencies particularly regarding solubility limits, and the actual test substance concentrations to which each species were exposed. Therefore, the study from which the data were extrapolated have limited reliability. In addition, surrogate 1,2-decanediol is more aquatically toxic than 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.

- *Fish*
  - No measured chronic toxicity data were found for caprylyl glycol or a similar surrogate.
  - Caprylyl glycol has surfactant properties and is not suitable for modeling with ECOSAR (U.S. EPA 2022).
  - In according with the U.S. EPA Sustainable Futures guidance, the ACR for estimating chronic toxicity of neutral organics is 10 for fish (U.S. EPA 2013). Therefore, the above specified LC_{50} of > 2.2 and ≤ 22 mg/L for acute exposures, divided by the ACR of 10, is 0.22 to 2.2 mg/L. Similarly, the LC_{50} of 14.1 mg/L for surrogate 1,2-decanediol, divided by the ACR of 10, is 1.41 mg/L.
- *Crustacea*
  - No measured chronic toxicity data were found for caprylyl glycol or a similar surrogate.
  - Caprylyl glycol has surfactant properties and is not suitable for modeling with ECOSAR (U.S. EPA 2022).
  - In according with the U.S. EPA Sustainable Futures guidance, the ACR for estimating chronic toxicity of neutral organics is 10 for daphnids (U.S. EPA 2013). Therefore, the above specified EC_{50} of 176 mg/L for acute exposures, divided by the ACR of 10, is 17.6 mg/L. Similarly, the EC_{50} of 25.5 mg/L for the surrogate 1,2-decanediol (CAS #1119-86-4) for acute exposures, divided by the ACR of 10, is 2.55 mg/L.
- *Algae*
  - ECHA, CAS #1117-86-8, 2024
    - As summarized previously, caprylyl glycol was evaluated in a GLP-compliant Algal Growth Inhibition Test performed according to OECD TG 201 and ISO 8692. *R. subcapitata* (green algae) were exposed to the test substance (purity not specified) at concentrations up to 200 mg/L (nominal) (measured concentrations were 76% of nominal at test start (equivalent to 152 mg/L based on carbon content), and 81-86% of nominal at test end (equivalent to 167 mg/L based on carbon content of 110 mg/L based on TOC)) for 72 hours under static conditions. The 72-hour NOEC based on growth rate was 15 mg/L (measured) (Klimisch 1, reliable without restrictions) (Unnamed 2007 study report). *ECHA discounted the reliability of this study in its dossier evaluation (ECHA 2022) on the basis that the test substance solubility was not adequately characterized, testing appeared to have been performed well above the solubility limits, and it was unclear if the algae were exposed to the test substance at concentrations below the CMC.*
  - ECHA, CAS #5343-92-0, 2024
    - 72-hour growth rate EC_{10} (*D. subspicatus*, green algae) = 5,477.33 (nominal) (non-GLP, DIN 38412 part 9) (Klimisch 2, reliable with restrictions) (Unmanned 1990 study report).
  - ECHA, CAS #1119-86-4, 2024
    - Surrogate data: As summarized previously, 1,2-decanediol (CAS #1119-86-4) was evaluated in a GLP-compliant Acute Immobilization Test performed according to OECD TG 201 and EU Method C.3. *R. subcapitata* (green algae) were exposed to the test substance (purity not specified) for 72 hours under static conditions at concentrations up to 100 mg/L (nominal), equivalent to 104 mg/L (measured in fresh and old medium). The 72-hour NOEC based on growth rate was 12.5 mg/L (nominal) (Klimisch 1, reliable without restrictions) (Unnamed 2015 study report).
- Based on the weight of evidence, a score of Moderate was assigned. No chronic data were identified for caprylyl glycol for the fish and crustacea trophic levels, and modeling with ECOSAR was not suitable for chemicals with surfactant properties. In addition, as previously discussed,

studies performed on caprylyl glycol were of limited reliability as determined by ECHA. Therefore, ToxServices relied on data on the conservative surrogate 1,2-decanediol, adjusted by the ACRs for their relevant trophic levels, to estimate chronic values. The most conservative chronic value is 1.41 mg/L for the fish trophic level, which lies within the Moderate range (1-10 mg/L).

Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): vL

Caprylyl glycol was assigned a score of Very Low for persistence based on measured data. Caprylyl glycol reached > 60% degradation, and met the 10-day window criterion in two studies (OECD TG 301 D / EU Method C.4-E and OECD TG 301F / EU Method C.4-D). GreenScreen® criteria classify chemicals as a Very Low hazard for persistence when a substance meets the criteria for ready biodegradability (> 60% degradation in 28 days, and meets the 10-day window). Confidence is high based on measured data for the target compound.

- 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 #1117-86-8, 2024
  - Caprylyl glycol was evaluated in a GLP-compliant Ready Biodegradability: Closed Bottle Test performed according to OECD TG 301 D and EU Method C.4-E. Domestic, non-adapted, activated sludge was exposed to the test substance (purity not specified) at 2 mg/L (nominal), equivalent to 5 mg/L theoretical oxygen demand (ThOD), under aerobic conditions, for 28 days. Biodegradation was measured based on oxygen consumption. The reference substance was sodium benzoate. The test substance reached 10% by day 8, 61% by day 14, and 75% degradation by day 28, and the reference substance performed as expected. The authors concluded that the test substance was readily biodegradable under the conditions of the test, and met the 10-day window (Klimisch 1, reliable without restrictions) (Unnamed 2003 study report).
  - Caprylyl glycol was evaluated in a GLP-compliant Ready Biodegradability: Manometric Respirometry Test performed according to OECD TG 301 F and EU Method C.4-D. Domestic, non-adapted, activated sludge was exposed to the test substance (purity not specified) at 100 mg/L (nominal), equivalent to 253 mg/L ThOD, under aerobic conditions, for 28 days. Biodegradation was measured based on oxygen consumption. The reference substance was sodium benzoate. The test substance reached 11% degradation by day 2, 61.5% by day 9, and 85% by day 28. The reference substance performed as expected. The authors concluded that the test substance was readily biodegradable under the conditions of the test, and met the 10-day window (Klimisch 1, reliable without restrictions) (Unnamed 2011 study report).

Bioaccumulation (B) Score (vH, H, M, L, or vL): vL

Caprylyl glycol was assigned a score of Very Low for bioaccumulation based on a measured Log K_{OW} of 2.1. GreenScreen® criteria classify chemicals as a Very Low hazard for bioaccumulation when the log K_{OW} is ≤ 4 (CPA 2018b). The confidence in the score is high based on a measured Log K_{OW}.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- Caprylyl glycol has surfactant properties and is not suitable for modeling with EPI Suite™ (U.S. EPA 2017).

- ECHA, CAS #1117-86-8, 2024
    - Caprylyl glycol has a measured log K_{OW} of 2.1 at 25°C and pH of 6 (OECD TG 117 and EU Method A.8).

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M, or L): *L*

Caprylyl glycol was assigned a score of Low for reactivity. It lacks reactive functional groups in its molecular structure that would be associated with explosivity and self-reactivity, it does not emit flammable gases on contact with water, is not oxidizing, is not a peroxide, is not self-heating, and does not require desensitization. GreenScreen® criteria classify chemicals as a Low hazard for reactivity when they are not explosive and not otherwise reactive (CPA 2018b). Confidence is low due to lack of experimental data. It may be noted that no data were found regarding corrosivity to metals.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.
- No measured data were identified. Therefore, screening procedures for explosivity were used here to estimate the reactivity property of caprylyl glycol. These procedures are listed in the GHS (UN 2023).
    - Based on the structure of its components or moieties, caprylyl glycol is not considered explosive or self-reactive due to lack of functional groups associated with explosive or self-reactive properties (See Appendix K).
    - Based on the structure of its components or moieties, caprylyl glycol 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, for organic substances which contain oxygen, fluorine, and/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 caprylyl glycol has 2 oxygens, which are both bonded only to carbon and hydrogen, classification is not warranted.
    - Caprylyl glycol does not require testing for self-ignition because it is a liquid.
    - Caprylyl glycol is soluble in water and is not noted for emitting flammable gases on contact with water.
    - As caprylyl glycol is not explosive, it does not require desensitization.

Flammability (F) Score (vH, H, M, or L): L

Caprylyl glycol was assigned a score of Low for flammability based on its lowest measured flash point of 109.1 +/- 13°C. This exceeds the GHS Category 4 guidance value of 93°C, and therefore GHS classification is not warranted. GreenScreen® criteria classify chemicals as a Low hazard for flammability when adequate data exist and GHS classification is not warranted (CPA 2018b). The confidence in the score was high based on measured 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 #1117-86-8, 2024
    - Caprylyl glycol has a flash point of 140.5°C when measured in a GLP-compliant closed cup method conducted according to EU A.9, and EPA OPPTS 830.6315.
- CIR 2012

- Caprylyl glycol is reported to have a calculated flash point of 109.1 ± 13.0°C (no further details provided).

Use of New Approach Methodologies (NAMs)[9] in the Assessment, Including Uncertainty Analyses of Input and Output

New Approach Methodologies (NAMs) used in this GreenScreen® include *in silico* modeling for carcinogenicity, endocrine activity, respiratory sensitization, and chronic aquatic toxicity, and *in vitro* data for mutagenicity, 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 caprylyl glycol's NAMs dataset include limited data for carcinogenicity, genotoxicity, endocrine activity, and chronic aquatic toxicity, and neither experimental data nor available validated test methods for respiratory sensitization. Caprylyl glycol's Type II (extrapolation output) uncertainties include use of structural alerts and modeling programs without defined applicability domains, reliance on *in vitro* assays to assess genotoxicity where the methods do not fully mimic *in vivo* metabolic conditions and only focus on a few events of the genotoxicity process, the uncertain *in vivo* relevance of *in silico* modeling and *in vitro* high throughput screening assays due to lack of consideration of toxicokinetics. the lack of consideration of non-immunologic mechanisms for respiratory sensitization when evaluating the structural alerts and the limitation of the hen's egg test-chorioallantoic membrane (HET-CAM) in identifying irritating substances that are not corrosive. Some of caprylyl glycol'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	**Carcinogenicity**: Only limited experimental data are available. **Genotoxicity:** Some of the experimental data has limited reporting; therefore, it is unclear if the testing was performed in accordance with the corresponding test guidelines. **Endocrine activity:** No *in vivo* data are available. **Respiratory sensitization**: No experimental data are available and there are no validated test methods. **Chronic aquatic toxicity:** No experimental data are available for the fish and crustacea trophic levels.
Type II Uncertainty: Extrapolation Output	**Carcinogenicity**: Toxtree only identifies structural alerts (SAs), and no applicability domain can be defined (Toxtree 2018).

[9] 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).

	Genotoxicity: The bacterial reverse mutation assay (as defined in OECD TG 471) only tests point-mutation inducing activity in non-mammalian cells, and the exogenous metabolic activation system does not entirely mimic *in vivo* conditions[10]. The mammalian cell gene mutation assay (as defined in OECD TG 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).[11] The *in vitro* chromosome aberration assay (OECD TG 473) does not measure aneuploidy and it only measures structural chromosomal aberrations. The exogenous metabolic activation system does not entirely mirror *in vivo* metabolism[12]. **Endocrine activity:** The *in vivo* relevance of *in silico* modeling and *in vitro* high throughput screening assays is uncertain due to lack of consideration of toxicokinetics. ToxCast models don't define applicability domain. **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 HET-CAM assay could only identify corrosive substances (GHS Category 1). It does not identify GHS Categories 2A or 2B irritants. Also, depending on regulatory context, this assay may be considered an animal test[13].
Endpoint	**NAMs Data Available and Evaluated? (Y/N)**	**Types of NAMs Data (*in silico* modeling/*in vitro* biological profiling/frameworks)**
Carcinogenicity	Y	*In silico* modeling: VEGA and Toxtree
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 silico* modeling: ToxCast

[10] https://www.oecd-ilibrary.org/docserver/9789264071247-en.pdf?expires=1614097593&id=id&accname=guest&checksum=89925F80B9F4BD2FFC6E90F94A0EE427
[11] https://www.oecd-ilibrary.org/docserver/9789264264809-en.pdf?expires=1614097800&id=id&accname=guest&checksum=C0DE371FB9C5A878E66C9AB7F84E6BBE
[12] https://www.oecd-ilibrary.org/docserver/9789264264649-en.pdf?expires=1614098015&id=id&accname=guest&checksum=6A4F9CE52EA974F5A74793DD54D54352
[13] https://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV-JM-MONO(2017)15/REV1%20&doclanguage=en

		In vitro data: High throughput screening tests
Acute mammalian toxicity	N	
Single exposure systemic toxicity	N	
Repeated exposure systemic toxicity	N	
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* data: HET-CAM
Acute aquatic toxicity	N	
Chronic aquatic toxicity	Y	Extrapolation from acute to chronic toxicity
Persistence	N	
Bioaccumulation	N	

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APPENDIX A: Hazard Classification Acronyms
(in alphabetical order)

(AA) Acute Aquatic Toxicity

(AT) Acute Mammalian Toxicity

(B) Bioaccumulat€

(C) Carcinogenicity

(CA) Chronic Aquatic Toxicity

(D) Developmental To€ity

(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 Caprylyl Glycol (CAS #1117-86-8)

TOXSERVICES
TOXICOLOGY RISK ASSESSMENT CONSULTING

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	Caprylyl glycol	1117-86-8	L	*L*	*L*	*M*	DG	L	L	L	M	L	L	*L*	L	H	*M*	*M*	vL	vL	*L*	L

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	No	No
3	STOP						
4	STOP						

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
Caprylyl glycol	2

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

Table 6

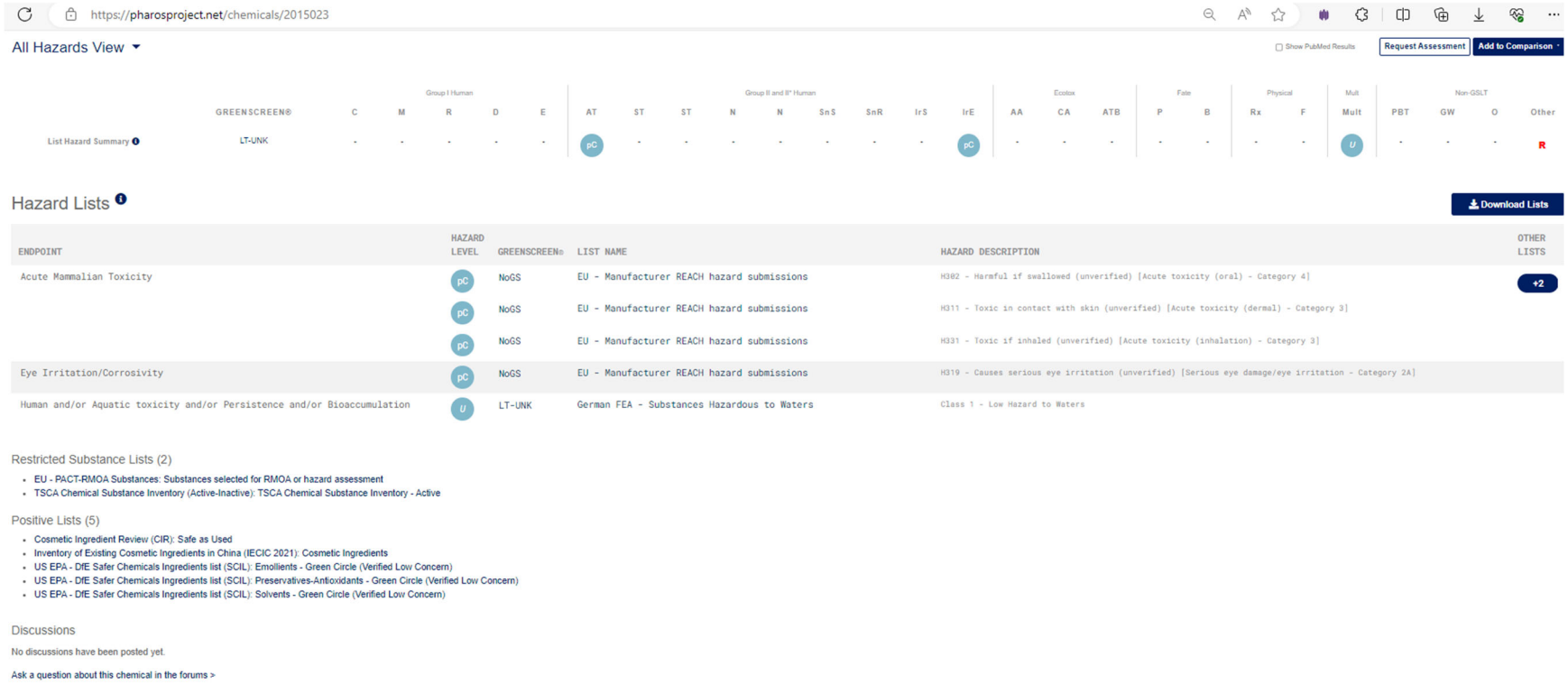
Chemical Name	Final GreenScreen® Benchmark Score
Caprylyl glycol	2

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 Caprylyl Glycol (CAS #1117-86-8)



https://pharosproject.net/chemicals/2015023

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	-	-	-	-	-	pC	-	-	-	-	-	-	-	pC	-	-	-	-	-	-	-	U	-	-	-	R

Hazard Lists

Download Lists

ENDPOINT	HAZARD LEVEL	GREENSCREEN®	LIST NAME	HAZARD DESCRIPTION	OTHER LISTS
Acute Mammalian Toxicity	pC	NoGS	EU - Manufacturer REACH hazard submissions	H302 - Harmful if swallowed (unverified) [Acute toxicity (oral) - Category 4]	+2
	pC	NoGS	EU - Manufacturer REACH hazard submissions	H311 - Toxic in contact with skin (unverified) [Acute toxicity (dermal) - Category 3]	
	pC	NoGS	EU - Manufacturer REACH hazard submissions	H331 - Toxic if inhaled (unverified) [Acute toxicity (inhalation) - Category 3]	
Eye Irritation/Corrosivity	pC	NoGS	EU - Manufacturer REACH hazard submissions	H319 - Causes serious eye irritation (unverified) [Serious eye damage/eye irritation - Category 2A]	
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 (2)

- EU - PACT-RMOA Substances: Substances selected for RMOA or hazard assessment
- TSCA Chemical Substance Inventory (Active-Inactive): TSCA Chemical Substance Inventory - Active

Positive Lists (5)

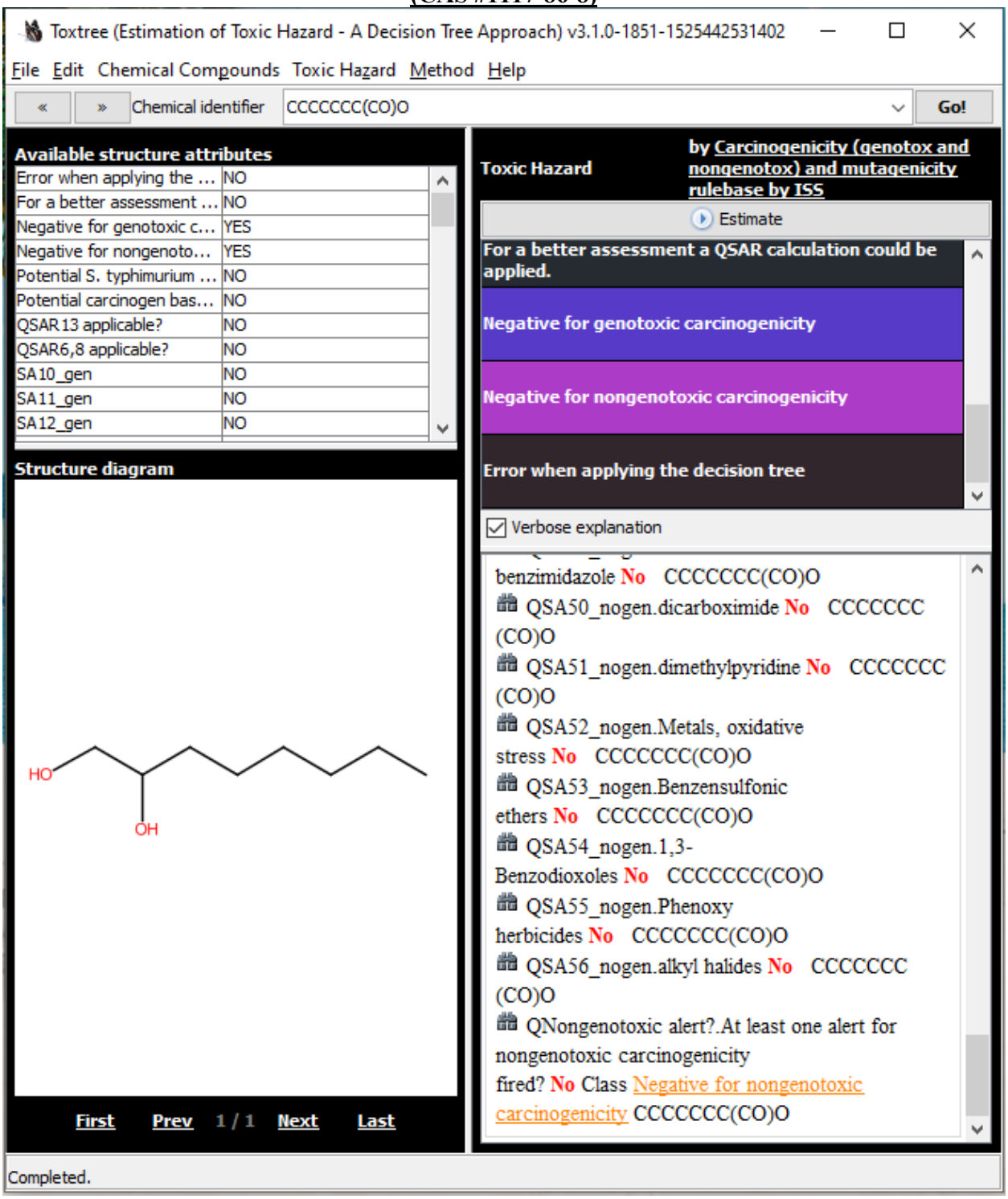
- Cosmetic Ingredient Review (CIR): Safe as Used
- Inventory of Existing Cosmetic Ingredients in China (IECIC 2021): Cosmetic Ingredients
- US EPA - DfE Safer Chemicals Ingredients list (SCIL): Emollients - Green Circle (Verified Low Concern)
- US EPA - DfE Safer Chemicals Ingredients list (SCIL): Preservatives-Antioxidants - Green Circle (Verified Low Concern)
- US EPA - DfE Safer Chemicals Ingredients list (SCIL): Solvents - Green Circle (Verified Low Concern)

Discussions

No discussions have been posted yet.

Ask a question about this chemical in the forums >

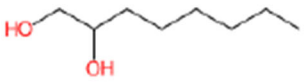
APPENDIX D: Toxtree Carcinogenicity Modeling results for Caprylyl Glycol (CAS #1117-86-8)



APPENDIX E: VEGA Skin Sensitization Results for Caprylyl glycol (CAS #1117-86-8)

1. Prediction Summary

Prediction for compound Molecule 0 -



Prediction: Reliability:

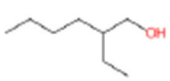
Prediction is NON-Carcinogen, but the result shows some critical aspects, which require to be checked:
- Accuracy of prediction for similar molecules found in the training set is not optimal

Compound: Molecule 0
Compound SMILES: OCC(O)CCCCCC
Experimental value: -
Predicted Carcinogen activity: NON-Carcinogen
P(Carcinogen): 0.134
P(NON-Carcinogen): 0.867
Reliability: The predicted compound could be out of the Applicability Domain of the model
Remarks:
none

3.1 Applicability Domain:
Similar Compounds, with Predicted and Experimental Values

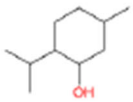
Compound #1

CAS: 35449-36-6
Dataset id:345 (Training Set)
SMILES: OCC(C)(C)CCCCCCC(C)(C)CO
Similarity: 0.891
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen



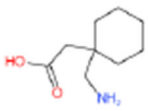
Compound #2

CAS: 104-76-7
Dataset id:314 (Training Set)
SMILES: OCC(CC)CCCC
Similarity: 0.879
Experimental value : NON-Carcinogen
Predicted value : Carcinogen



Compound #3

CAS: 89-78-1
Dataset id:427 (Training Set)
SMILES: OC1CC(C)CCC1(C(C)C)
Similarity: 0.846
Experimental value : NON-Carcinogen
Predicted value : Carcinogen



Compound #4

CAS: 60142-96-3
Dataset id:48 (Training Set)
SMILES: O=C(O)CC1(CN)(CCCCC1)
Similarity: 0.814
Experimental value : Carcinogen
Predicted value : Carcinogen

Compound #5

CAS: 2432-99-7
Dataset id:50 (Test Set)
SMILES: O=C(O)CCCCCCCCCCN
Similarity: 0.813
Experimental value : Carcinogen
Predicted value : NON-Carcinogen

Compound #6

CAS: 57-55-6
Dataset id:677 (Training Set)
SMILES: OCC(O)C
Similarity: 0.808
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen

3.2 Applicability Domain:
Measured Applicability Domain Scores

⚠	Global AD Index AD index = 0.793 Explanation: The predicted compound could be out of the Applicability Domain of the model.
✓	Similar molecules with known experimental value Similarity index = 0.885 Explanation: Strongly similar compounds with known experimental value in the training set have been ..
⚠	Accuracy of prediction for similar molecules Accuracy index = 0.504 Explanation: Accuracy of prediction for similar molecules found in the training set is not optimal..
✓	Concordance for similar molecules Concordance index = 1 Explanation: Similar molecules found in the training set have experimental values that agree with the predicted value..
✓	Model's descriptors range check Descriptors range check = True Explanation: descriptors for this compound have values inside the descriptor range of the compounds of the training set..
✓	Atom Centered Fragments similarity check ACF index = 1 Explanation: all atom centered fragment of the compound have been found in the compounds of the training set..
✓	Model class assignment reliability Pos/Non-Pos difference = 0.733 Explanation: model class assignment is well defined..
✓	Neural map neurons concordance Neurons concordance = 1 Explanation: predicted value agrees with experimental values of training set compounds laying in the same neuron..

Symbols explanation:

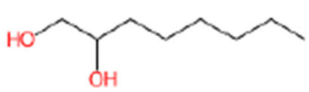
✓ The feature has a good assessment, model is reliable regarding this aspect.

⚠ The feature has a non optimal assessment, this aspect should be reviewed by an expert.

✗ The feature has a bad assessment, model is not reliable regarding this aspect.

1. Prediction Summary

Prediction for compound Molecule 0 -

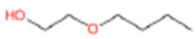


Prediction: Reliability:

Prediction is NON-Carcinogen, but the result may be not reliable. A check of the information given in the following section should be done, paying particular attention to the following issues:
- Accuracy of prediction for similar molecules found in the training set is not adequate
- similar molecules found in the training set have experimental values that disagree with the predicted value

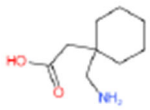
Compound: Molecule 0
Compound SMILES: OCC(O)CCCCCC
Experimental value: -
Predicted Carcinogen activity: NON-Carcinogen
Structural Alerts: -
Reliability: The predicted compound is outside the Applicability Domain of the model
Remarks:
none

3.1 Applicability Domain:
Similar Compounds, with Predicted and Experimental Values



Compound #1

CAS: 111-76-2
Dataset id:596 (Training Set)
SMILES: OCCOCCCC
Similarity: 0.819
Experimental value : Carcinogen
Predicted value : NON-Carcinogen

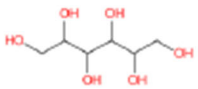


Compound #2

CAS: 60142-96-3
Dataset id:789 (Training Set)
SMILES: O=C(O)CC1(CN)(CCCCC1)
Similarity: 0.814
Experimental value : Carcinogen
Predicted value : NON-Carcinogen

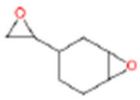
Compound #3

CAS: 2432-99-7
Dataset id:36 (Training Set)
SMILES: O=C(O)CCCCCCCCCCN
Similarity: 0.813
Experimental value : Carcinogen
Predicted value : NON-Carcinogen



Compound #4

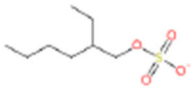
CAS: 69-65-8
Dataset id:86 (Training Set)
SMILES: OCC(O)C(O)C(O)C(O)CO
Similarity: 0.792
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen



Compound #5

CAS: 106-87-6
Dataset id:608 (Training Set)
SMILES: O1CC1C2CCC3OC3(C2)
Similarity: 0.761
Experimental value : Carcinogen
Predicted value : Carcinogen

Alerts (not found also in the target): SA7 Epoxides and aziridines



Compound #6

CAS: 126-92-1
Dataset id:77 (Training Set)
SMILES: O=S(=O)([O-])OCC(CC)CCCC
Similarity: 0.755
Experimental value : Carcinogen
Predicted value : Carcinogen

Alerts (not found also in the target): SA41 Substituted n-alkylcarboxylic acids

3.2 Applicability Domain:
Measured Applicability Domain Scores

✖	Global AD Index AD index = 0 Explanation: The predicted compound is outside the Applicability Domain of the model.
✔	Similar molecules with known experimental value Similarity index = 0.816 Explanation: Strongly similar compounds with known experimental value in the training set have been ..
✖	Accuracy of prediction for similar molecules Accuracy index = 0 Explanation: Accuracy of prediction for similar molecules found in the training set is not adequate..
✖	Concordance for similar molecules Concordance index = 0 Explanation: similar molecules found in the training set have experimental values that disagree with the predicted value..
✔	Atom Centered Fragments similarity check ACF index = 1 Explanation: all atom centered fragment of the compound have been found in the compounds of the training set..

Symbols explanation:

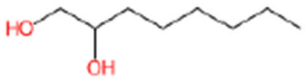
✔ The feature has a good assessment, model is reliable regarding this aspect.

⚠ The feature has a non optimal assessment, this aspect should be reviewed by an expert.

✖ The feature has a bad assessment, model is not reliable regarding this aspect.

1. Prediction Summary

Prediction for compound Molecule 0 -

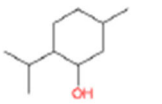


Prediction: Reliability:

Prediction is Possible NON-Carcinogen, but the result may be not reliable. A check of the information given in the following section should be done, paying particular attention to the following issues:
- Accuracy of prediction for similar molecules found in the training set is not adequate
- similar molecules found in the training set have experimental values that disagree with the predicted value

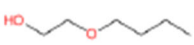
Compound: Molecule 0
Compound SMILES: OCC(O)CCCCCC
Experimental value: -
Predicted Carcinogenic activity: Possible NON-Carcinogen
No. alerts for carcinogenicity: 0
Structural Alerts: -
Reliability: The predicted compound is outside the Applicability Domain of the model
Remarks:
none

3.1 Applicability Domain:
Similar Compounds, with Predicted and Experimental Values



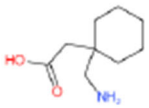
Compound #1

CAS: 15356-70-4
Dataset id:654 (Training Set)
SMILES: OC1CC(C)CCC1(C(C)C)
Similarity: 0.846
Experimental value : NON-Carcinogen
Predicted value : Possible NON-Carcinogen



Compound #2

CAS: 111-76-2
Dataset id:498 (Training Set)
SMILES: OCCOCCCC
Similarity: 0.819
Experimental value : Carcinogen
Predicted value : Possible NON-Carcinogen

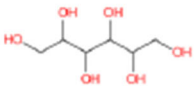


Compound #3

CAS: 60142-96-3
Dataset id:725 (Training Set)
SMILES: O=C(O)CC1(CN)(CCCCC1)
Similarity: 0.814
Experimental value : Carcinogen
Predicted value : Possible NON-Carcinogen

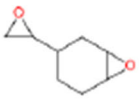
Compound #4

CAS: 2432-99-7
Dataset id:29 (Training Set)
SMILES: O=C(O)CCCCCCCCCCCN
Similarity: 0.813
Experimental value : Carcinogen
Predicted value : Possible NON-Carcinogen



Compound #5

CAS: 69-65-8
Dataset id:69 (Training Set)
SMILES: OCC(O)C(O)C(O)C(O)CO
Similarity: 0.792
Experimental value : NON-Carcinogen
Predicted value : Possible NON-Carcinogen



Compound #6

CAS: 106-87-6
Dataset id:685 (Training Set)
SMILES: O1CC1C2CCC3OC3(C2)
Similarity: 0.761
Experimental value : Carcinogen
Predicted value : Carcinogen

Alerts (not found also in the target): Carcinogenity alert no. 23; Carcinogenity alert no. 29

3.2 Applicability Domain:
Measured Applicability Domain Scores

✖	Global AD Index AD index = 0.532 Explanation: The predicted compound is outside the Applicability Domain of the model.
✔	Similar molecules with known experimental value Similarity index = 0.825 Explanation: Strongly similar compounds with known experimental value in the training set have been ..
✖	Accuracy of prediction for similar molecules Accuracy index = 0.343 Explanation: Accuracy of prediction for similar molecules found in the training set is not adequate..
✖	Concordance for similar molecules Concordance index = 0.343 Explanation: similar molecules found in the training set have experimental values that disagree with the predicted value..
✔	Atom Centered Fragments similarity check ACF index = 1 Explanation: all atom centered fragment of the compound have been found in the compounds of the training set..

Symbols explanation:

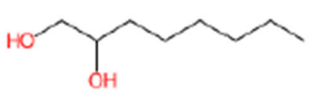
✔ The feature has a good assessment, model is reliable regarding this aspect.

⚠ The feature has a non optimal assessment, this aspect should be reviewed by an expert.

✖ The feature has a bad assessment, model is not reliable regarding this aspect.

1. Prediction Summary

Prediction for compound Molecule 0 -



Prediction: Reliability:

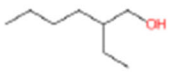
Prediction is Possible NON-Carcinogen, the result appears reliable. Anyhow, you should check it through the evaluation of the information given in the following sections.

Compound: Molecule 0
Compound SMILES: OCC(O)CCCCCC
Experimental value: -
Predicted Carcinogenic activity: Possible NON-Carcinogen
No. alerts for carcinogenicity: 0
Structural Alerts: -
Reliability: The predicted compound is into the Applicability Domain of the model
Remarks:
none

3.1 Applicability Domain:
Similar Compounds, with Predicted and Experimental Values

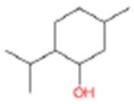
Compound #1

CAS: 35449-36-6
Dataset id:345 (Training Set)
SMILES: OCC(C)(C)CCCCCCC(C)(C)CO
Similarity: 0.891
Experimental value : NON-Carcinogen
Predicted value : Possible NON-Carcinogen



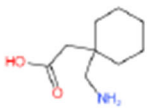
Compound #2

CAS: 104-76-7
Dataset id:314 (Training Set)
SMILES: OCC(CC)CCCC
Similarity: 0.879
Experimental value : NON-Carcinogen
Predicted value : Possible NON-Carcinogen



Compound #3

CAS: 89-78-1
Dataset id:427 (Training Set)
SMILES: OC1CC(C)CCC1(C(C)C)
Similarity: 0.846
Experimental value : NON-Carcinogen
Predicted value : Possible NON-Carcinogen



Compound #4

CAS: 60142-96-3
Dataset id:48 (Training Set)
SMILES: O=C(O)CC1(CN)(CCCCC1)
Similarity: 0.814
Experimental value : Carcinogen
Predicted value : Possible NON-Carcinogen

Compound #5

CAS: 2432-99-7
Dataset id:50 (Test Set)
SMILES: O=C(O)CCCCCCCCCCN
Similarity: 0.813
Experimental value : Carcinogen
Predicted value : Possible NON-Carcinogen

Compound #6

CAS: 57-55-6
Dataset id:677 (Training Set)
SMILES: OCC(O)C
Similarity: 0.808
Experimental value : NON-Carcinogen
Predicted value : Possible NON-Carcinogen

3.2 Applicability Domain:
Measured Applicability Domain Scores

✓	Global AD Index AD index = 0.933 Explanation: The predicted compound is into the Applicability Domain of the model.
✓	Similar molecules with known experimental value Similarity index = 0.87 Explanation: Strongly similar compounds with known experimental value in the training set have been ..
✓	Accuracy of prediction for similar molecules Accuracy index = 1 Explanation: Accuracy of prediction for similar molecules found in the training set is good..
✓	Concordance for similar molecules Concordance index = 1 Explanation: Similar molecules found in the training set have experimental values that agree with the predicted value..
✓	Atom Centered Fragments similarity check ACF index = 1 Explanation: all atom centered fragment of the compound have been found in the compounds of the training set..

Symbols explanation:

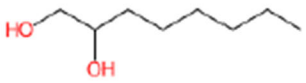
✓ The feature has a good assessment, model is reliable regarding this aspect.

⚠ The feature has a non optimal assessment, this aspect should be reviewed by an expert.

✗ The feature has a bad assessment, model is not reliable regarding this aspect.

1. Prediction Summary

Prediction for compound Molecule 0 -



Prediction: Reliability:

Prediction is Carcinogen, but the result may be not reliable. A check of the information given in the following section should be done, paying particular attention to the following issues:
- similar molecules found in the training set have experimental values that disagree with the predicted value

Compound: Molecule 0
Compound SMILES: OCC(O)CCCCCC
Experimental value: -
Predicted Oral Carcinogenic class: Carcinogen
Reliability: The predicted compound is outside the Applicability Domain of the model
Remarks:
none

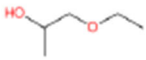
3.1 Applicability Domain:
Similar Compounds, with Predicted and Experimental Values

Compound #1

CAS: 111-76-2
Dataset id:509 (Training Set)
SMILES: OCCOCCCC
Similarity: 0.819
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen

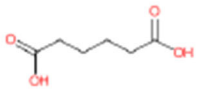
Compound #2

CAS: 57-55-6
Dataset id:661 (Training Set)
SMILES: OCC(O)C
Similarity: 0.808
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen



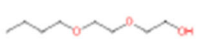
Compound #3

CAS: 1569-02-4
Dataset id:663 (Training Set)
SMILES: OC(C)COCC
Similarity: 0.789
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen



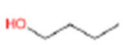
Compound #4

CAS: 124-04-9
Dataset id:541 (Training Set)
SMILES: O=C(O)CCCCC(=O)O
Similarity: 0.787
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen



Compound #5

CAS: 112-34-5
Dataset id:453 (Test Set)
SMILES: OCCOCCOCCCC
Similarity: 0.786
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen



Compound #6

CAS: 71-36-3
Dataset id:362 (Training Set)
SMILES: OCCCC
Similarity: 0.778
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen

3.2 Applicability Domain:
Measured Applicability Domain Scores

✖	Global AD Index AD index = 0 Explanation: The predicted compound is outside the Applicability Domain of the model.
✔	Similar molecules with known experimental value Similarity index = 0.813 Explanation: Strongly similar compounds with known experimental value in the training set have been ..
✔	Accuracy of prediction for similar molecules Accuracy index = 1 Explanation: Accuracy of prediction for similar molecules found in the training set is good..
✖	Concordance for similar molecules Concordance index = 0 Explanation: similar molecules found in the training set have experimental values that disagree with the predicted value..
✔	Model's descriptors range check Descriptors range check = True Explanation: descriptors for this compound have values inside the descriptor range of the compounds of the training set..
✔	Atom Centered Fragments similarity check ACF index = 1 Explanation: all atom centered fragment of the compound have been found in the compounds of the training set..

Symbols explanation:

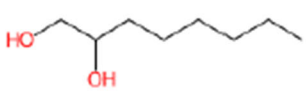
✔ The feature has a good assessment, model is reliable regarding this aspect.

⚠ The feature has a non optimal assessment, this aspect should be reviewed by an expert.

✖ The feature has a bad assessment, model is not reliable regarding this aspect.

1. Prediction Summary

Prediction for compound Molecule 0 -

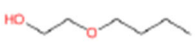


Prediction: Reliability:

Prediction is NON-Carcinogen, the result appears reliable. Anyhow, you should check it through the evaluation of the information given in the following sections.

Compound: Molecule 0
Compound SMILES: OCC(O)CCCCCC
Experimental value: -
Predicted Inhalation Carcinogenic class: NON-Carcinogen
Reliability: The predicted compound is into the Applicability Domain of the model
Remarks:
none

3.1 Applicability Domain:
Similar Compounds, with Predicted and Experimental Values

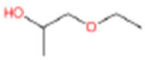


Compound #1

CAS: 111-76-2
Dataset id:482 (Training Set)
SMILES: OCCOCCCC
Similarity: 0.819
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen

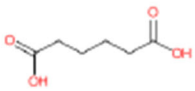
Compound #2

CAS: 57-55-6
Dataset id:650 (Test Set)
SMILES: OCC(O)C
Similarity: 0.808
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen



Compound #3

CAS: 1569-02-4
Dataset id:652 (Training Set)
SMILES: OC(C)COCC
Similarity: 0.789
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen



Compound #4

CAS: 124-04-9
Dataset id:517 (Training Set)
SMILES: O=C(O)CCCCC(=O)O
Similarity: 0.787
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen

Compound #5

CAS: 112-34-5
Dataset id:420 (Test Set)
SMILES: OCCOCCOCCCC
Similarity: 0.786
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen

Compound #6

CAS: 71-36-3
Dataset id:314 (Training Set)
SMILES: OCCCC
Similarity: 0.778
Experimental value : NON-Carcinogen
Predicted value : NON-Carcinogen

3.2 Applicability Domain:
Measured Applicability Domain Scores

✓	Global AD Index AD index = 0.902 Explanation: The predicted compound is into the Applicability Domain of the model.
✓	Similar molecules with known experimental value Similarity index = 0.813 Explanation: Strongly similar compounds with known experimental value in the training set have been ..
✓	Accuracy of prediction for similar molecules Accuracy index = 1 Explanation: Accuracy of prediction for similar molecules found in the training set is good..
✓	Concordance for similar molecules Concordance index = 1 Explanation: Similar molecules found in the training set have experimental values that agree with the predicted value..
✓	Model's descriptors range check Descriptors range check = True Explanation: descriptors for this compound have values inside the descriptor range of the compounds of the training set..
✓	Atom Centered Fragments similarity check ACF index = 1 Explanation: all atom centered fragment of the compound have been found in the compounds of the training set..

Symbols explanation:

✓ The feature has a good assessment, model is reliable regarding this aspect.

⚠ The feature has a non optimal assessment, this aspect should be reviewed by an expert.

✗ The feature has a bad assessment, model is not reliable regarding this aspect.

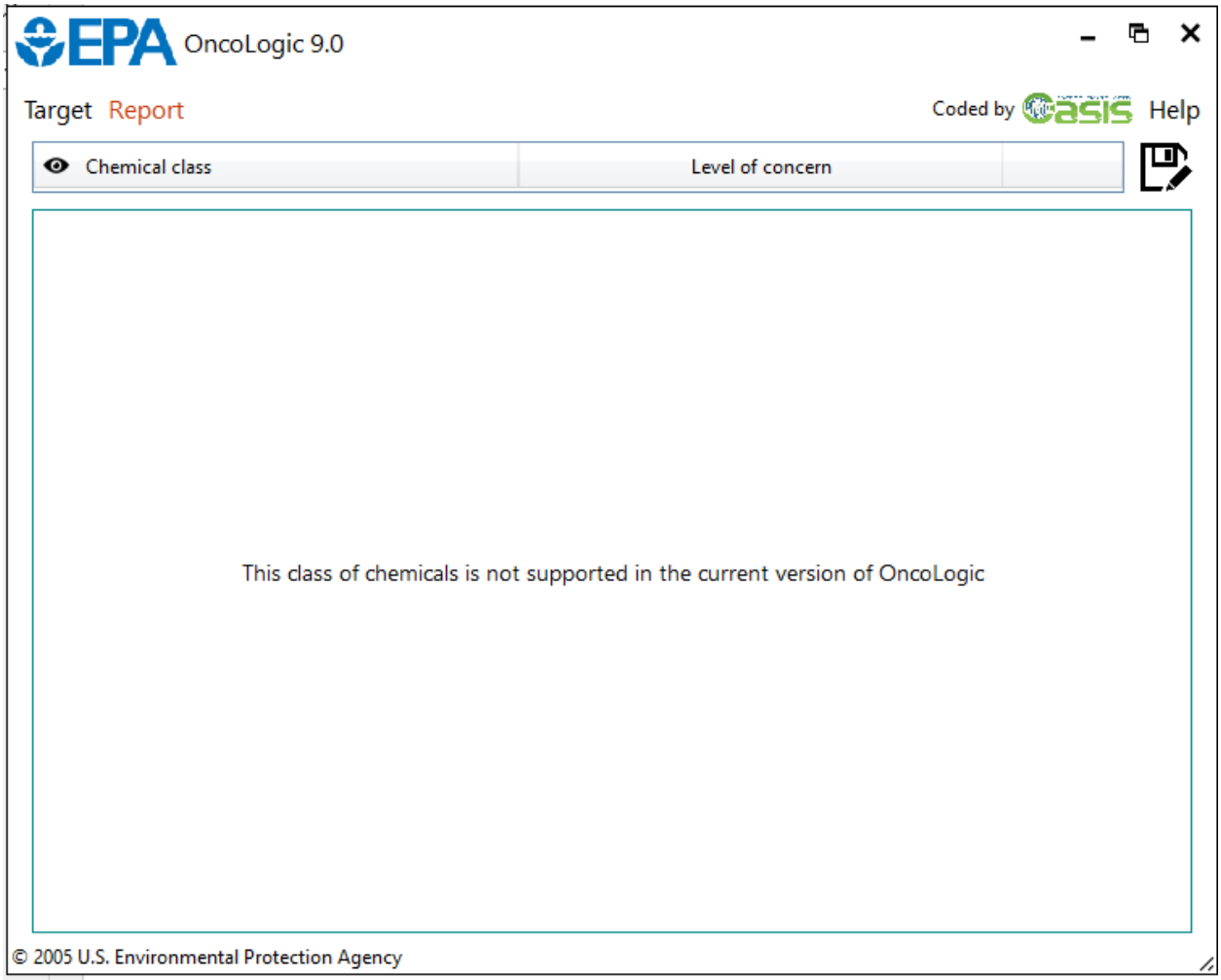
APPENDIX F: Danish QSAR Database Carcinogenicity Results for Caprylyl Glycol (CAS #1117-86-8)

Carcinogenicity

	E Ultra	Leadscope
FDA RCA Cancer Male Rat	POS_OUT	NEG_OUT
FDA RCA Cancer Female Rat	NEG_IN	NEG_IN
FDA RCA Cancer Rat	NEG_IN	INC_OUT
FDA RCA Cancer Male Mouse	NEG_IN	NEG_OUT
FDA RCA Cancer Female Mouse	NEG_IN	NEG_OUT
FDA RCA Cancer Mouse	NEG_IN	NEG_IN
FDA RCA Cancer Rodent	NEG_IN	INC_OUT
Commercial models from CASE Ultra and Leadscope		
FDA RCA: Data from US Food and Drug Administration as part of Research Cooperation Agreement		
Carcinogenicity (genotox and nongenotox) alerts by ISS, alerts in:		
- parent only	No alert found	
Oncologic Primary Classification, alerts in:		
- parent only	Not classified	
OECD QSAR Toolbox v.4.2 profilers		
Profiler predictions are supporting information to be used together with the relevant QSAR predictions		

	Exp	Battery	CASE Ultra	Leadscope	SciQSAR
Liver Specific Cancer in Rat or Mouse		NEG_IN	NEG_IN	NEG_IN	NEG_OUT
DTU-developed models					

APPENDIX G: OncoLogic Carcinogenicity Results for Caprylyl Glycol (CAS #5343-92-0)



OncoLogic Justification Report

SUMMARY :

CODE NUMBER : 1117868

SUBSTANCE ID :

JUSTIFICATION:

Aliphatic Alcohols*

Aliphatic alcohols (R-OH) may be loosely divided into (a) high M.W. alcohols (C > 20), (b) medium size alcohols (C = 6 to 20), and (c) low M.W. alcohols (C < 6). In general, high M.W. aliphatic alcohols have low potential to be significant carcinogens. A number of medium size alcohols (e.g., CF3(CF2)6CH2OH; 2-ethylhexanol) that can be oxidized to metabolically persistent aliphatic carboxylic acids (e.g., perfluorinated fatty acid like perfluoroooctanoic; ω – 1 branched fatty acids like 2-ethylhexanoic acid) are potential nongenotoxic carcinogens. Most of these are medium sized with the most potent ones peaking around 7 – 9 carbons. Low M.W. alcohols, (especially methanol and ethanol) are of carcinogenic concern because of possible oxidation to reactive aldehydes. The concern for carcinogenic risk is especially higher in individuals who are genetically deficient in aldehyde dehydrogenase which detoxifies aldehydes to carboxylic acids. A number of low M.W. tertiary alcohols (e.g., t-butyl, t-amyl) have been shown to induce kidney tumors in male rats by a mechanism (alpha-2-mu nephropathy) not relevant to humans. In addition, low M.W. alcohols with

(i) terminal double bond or Cl/Br/I,
(ii) α,β-unsaturation,
(iii) monosubstitution with Cl/Br/I at α-carbon are of concern as potential genotoxic carcinogens.

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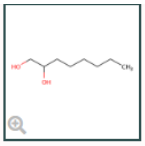
*This is only a brief summary of the structure activity relationships (SAR) knowledge of this class. A more detailed decision logic will be developed in future version of OncoLogic. If the compound of your interest has been tested in any short-term predictive tests, the results of the tests should be entered into OncoLogic's Functional Arm to give an evaluation of carcinogenic potential based on short-term predictive tests.

APPENDIX H: Tox21 EDSP Assays for Caprylyl Glycol (CAS #1117-86-8)

Name	Assay Lists	Details	SeqAPASS	Gene Symbol	AOP	Event	Repr. Plot	All Plots	Hit Call	Continuous Hit Call	Top	AC50
				ESR								
ATG_ERE_CIS	EDSP ER			ESR1	-	-			Inactive	-	-0.2	2.01
TOX21_ERa_BLA_Agonist_rati	EDSP ER			ESR1	-	-			Inactive	-	0	40
ATG_ERa_TRANS	EDSP ER			ESR1	-	-			Inactive	0	0	100
TOX21_ERa_BLA_Antagonist_	EDSP ER			ESR1	-	-			Inactive	0	0	40
ACEA_ER_80hr	EDSP ER			ESR1	220	1394			Inactive	0	0	50
TOX21_ERa_LUC_VM7_Antag	EDSP ER			ESR1	-	-			Inactive	-	-	-
TOX21_ERa_LUC_VM7_Agonis	EDSP ER			ESR1	-	-			Inactive	-	1.34	0
ATG_AR_TRANS	EDSP AR			AR	-	-			Inactive	0	0.08	100
TOX21_AR_LUC_MDAKB2_Ag	EDSP AR			AR	23	25			Inactive	-	0	45
TOX21_AR_LUC_MDAKB2_An	EDSP AR			AR	-	-			Inactive	0	0	45
TOX21_AR_LUC_MDAKB2_An	EDSP AR			AR	-	-			Inactive	0	0	45
TOX21_AR_BLA_Agonist_ratio	EDSP AR			AR	23	25			Inactive	-	1.62	0.01
TOX21_AR_BLA_Antagonist_r	EDSP AR			AR	-	-			Inactive	0	0	40
TOX21_Aromatase_Inhibition	EDSP steroidogenesis			CYP19A1	25	36			Inactive	0	0	45
TOX21_TRA_COA_Agonist_Fo	EDSP thyroid			THRA	-	-			Inactive	-	-	-
TOX21_TRB_BLA_Agonist_Foll	EDSP thyroid			THRB	-	-			Inactive	-	-	-
TOX21_TR_LUC_GH3_Antagor	EDSP thyroid			THRA | THRB	-	-			Inactive	0	0	45
TOX21_TRB_COA_Agonist_Fo	EDSP thyroid			THRB	-	-			Inactive	-	-	-
TOX21_TR_LUC_GH3_Agonist	EDSP thyroid			THRA | THRB	-	-			Inactive	-	4.11	3.43
ATG_THRa1_TRANS	EDSP thyroid			THRA	-	-			Inactive	0	0	100
TOX21_TR_LUC_GH3_Agonist	EDSP thyroid			THRA | THRB	-	-			Inactive	-	3.67	2.17
TOX21_TSHR_HTRF_Antagoni	EDSP thyroid			TSHR	42 | 54 | 159	277			Inactive	-	0	45
TOX21_TSHR_HTRF_Agonist_r	EDSP thyroid			TSHR	42 | 54 | 159	277			Inactive	0	2.77	45
TOX21_TSHR_wt_Agonist_HTF	EDSP thyroid			TSHR	-	-			Inactive	-	1.88	0.02

APPENDIX I: ToxCast Endocrine Activity Modeling Results for Caprylyl Glycol (CAS #1117-86-8)



1,2-Octanediol

1117-86-8 | DTXSID9036646

Searched by CASRN

Bioactivity - ToxCast: Models

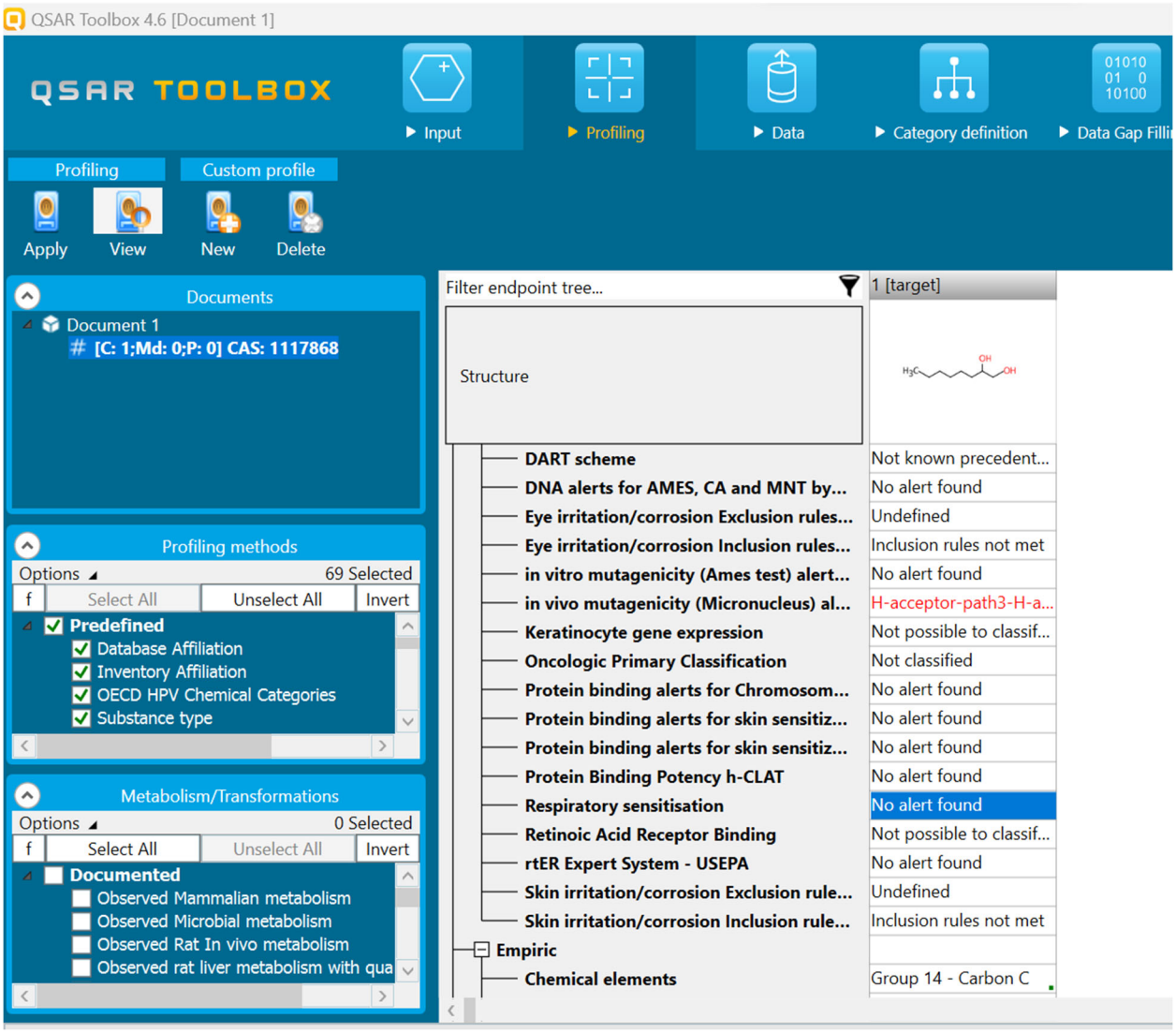
Export Data

EXPORT

ToxCast Model Predictions

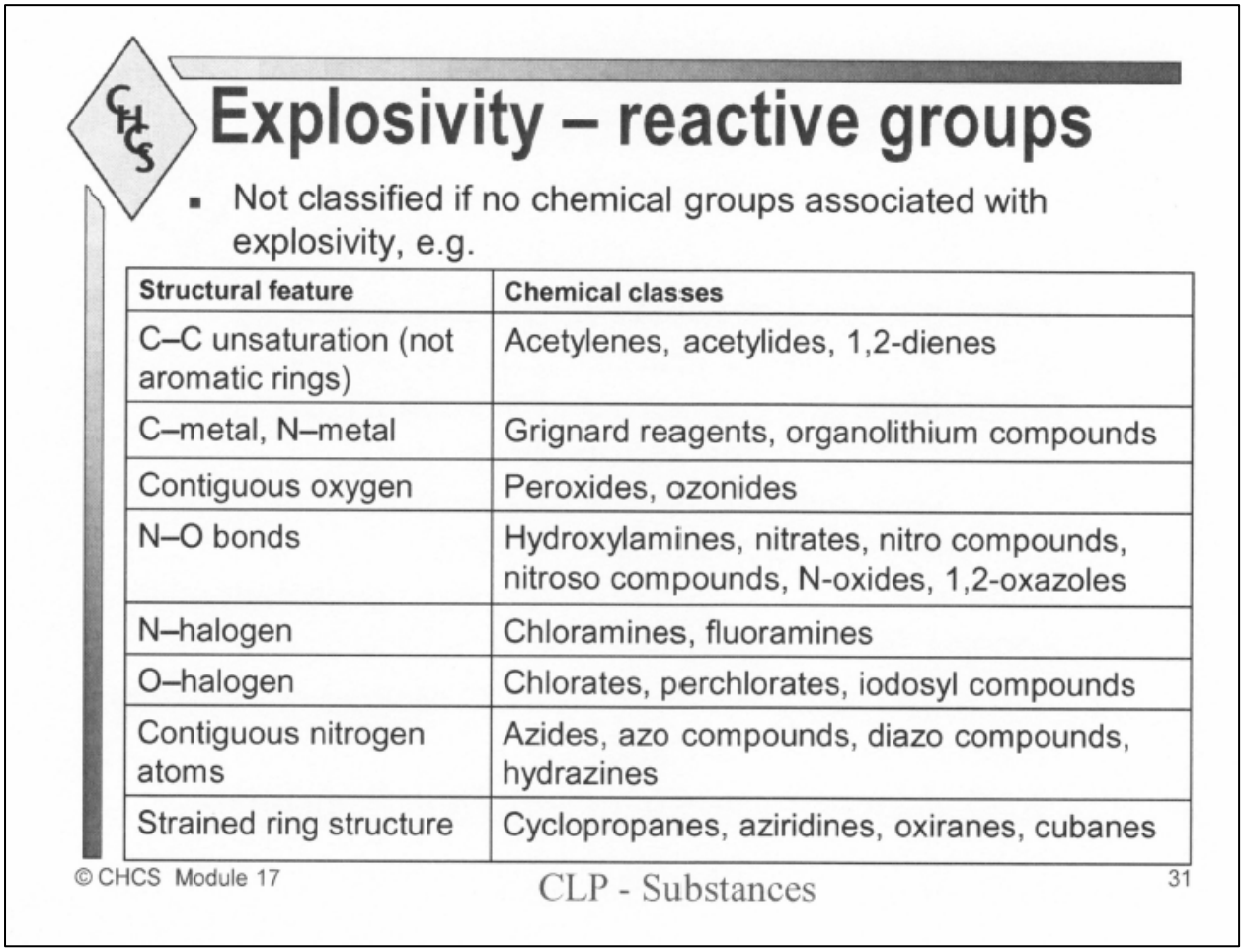
Model	Receptor	Agonist	Antagonist
CERAPP Potency Level (Consensus)	Estrogen	0.00	0.00
COMPARA (Consensus)	Androgen	0.00	0.00
CERAPP Potency Level (From Literature)	Estrogen	Inactive	Inactive

APPENDIX J: OECD Toolbox Profiling Results for Caprylyl Glycol (CAS #1117-86-8)



APPENDIX K: 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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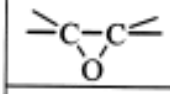
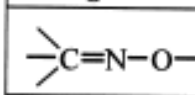
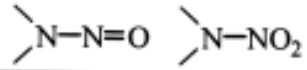
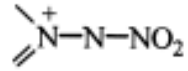
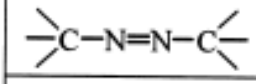
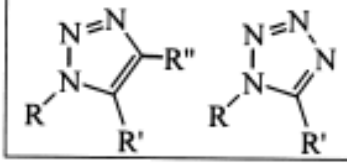
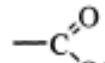
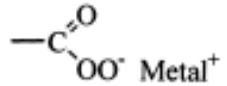
Explosivity – Full List

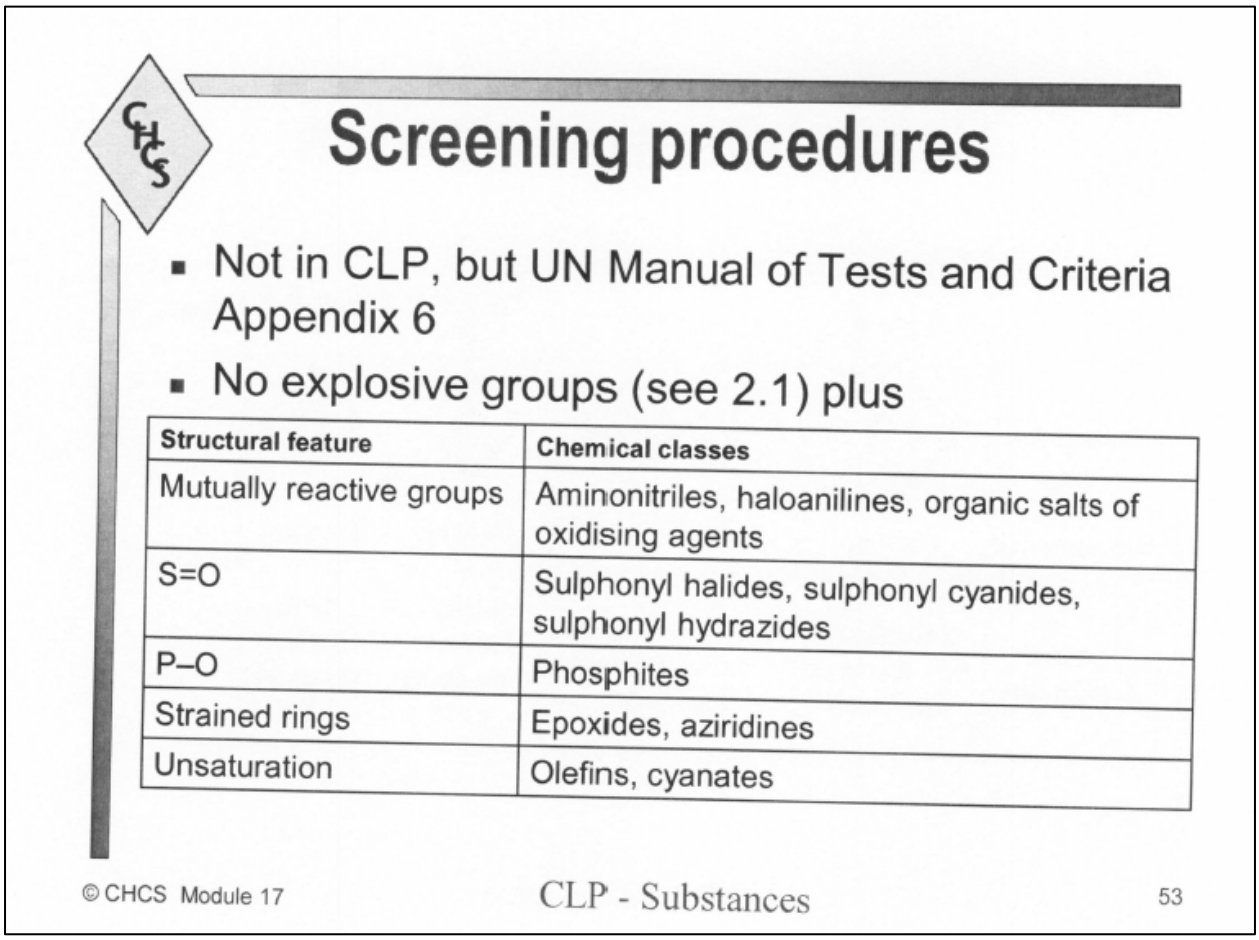
Table R.7.1-28 Chemical groups associated with explosive properties

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 L: Change in Benchmark Score

Table 5 provides a summary of changes to the GreenScreen® Benchmark™ for caprylyl glycol. The GreenScreen® Benchmark Score for caprylyl glycol has changed over time. The original GreenScreen® assessment was performed in 2015 under version 1.2 criteria and ToxServices assigned a Benchmark 3 (BM-3) score. Most recently in 2024, ToxServices changed the GreenScreen® benchmark score to a BM-2 due to reclassification of the developmental toxicity endpoints in the presence of new data.

Table 5: Change in GreenScreen® Benchmark™ for Caprylyl Glycol

Date	GreenScreen® Benchmark™	GreenScreen® Version	Comment
April 7, 2015	BM-3	v. 1.2	Original screen
February 22, 2024	BM-2	v. 1.4	BM score changed to a BM-2 due to reclassification of developmental toxicity endpoint, changing from Low hazard (high confidence) rating based on surrogate data, to a *Moderate* hazard (low confidence) based on measured data for the target compound.
March 18, 2024	BM-2	v. 1.4	BM unchanged. Improved clarity in response to comments from WA Department of Ecology.

Licensed GreenScreen® Profilers

Caprylyl Glycol GreenScreen® v. 1.2 Evaluation Prepared by:

SIGNATURE BLOCK

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Toxicologist
ToxServices LLC

Caprylyl Glycol GreenScreen® v. 1.2 Evaluation QC'd by:

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Bingxuan Wang, Ph.D.
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ToxServices LLC

Caprylyl Glycol GreenScreen® v. 1.4 Evaluation Update Prepared by:

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Caprylyl Glycol GreenScreen® v. 1.4 Update QC'd by:

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