PROPYLENE CARBONATE

(CAS #108-32-7)

GREENSCREEN® FOR SAFER CHEMICALS (GREENSCREEN®) ASSESSMENT

Prepared by:

ToxServices LLC

Assessment Date: June 16, 2021

Expiration Date: June 16, 2026

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GreenScreen® Executive Summary for Propylene Carbonate (CAS #108-32-7)

Propylene carbonate is a cyclic carbonate ester derived from propylene glycol. It is a colorless, odorless liquid and functions primarily as a solvent, auxiliary chemical, electrolyte in lithium batteries, and as a plasticizer. Propylene carbonate is used in cosmetics, paints, and some adhesives. It is used in a variety of formulations to improve performance and reduce volatile organic compounds (VOCs) and toxicity.

Propylene carbonate was assigned a **GreenScreen Benchmark™ Score of 3** ("Use but Still Opportunity for Improvement"). This score is based on the following hazard score combinations:

- Benchmark 3c
    - Moderate Group II Human Toxicity (skin irritation-IrS and single dose neurotoxicity-Ns)
    - High Group II Human Toxicity (eye irritation-IrE)

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), propylene carbonate meets requirements for a GreenScreen Benchmark™ Score of 3 despite the hazard data gap. In a worst-case scenario, if propylene carbonate were assigned a High score for the data gap E, it would be categorized as a Benchmark 1 Chemical.

New Approach Methodologies (NAMs) used in this GreenScreen® include *in silico* modeling for endocrine activity, skin sensitization, respiratory sensitization, chronic aquatic toxicity, and bioaccumulation, and *in vitro* assays for mutagenicity and endocrine activity. 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 propylene carbonate's NAMs dataset include no or lack of adequate experimental or human data for endocrine activity, skin sensitization, respiratory sensitization, and chronic aquatic toxicity. Propylene carbonate's Type II (extrapolation output) uncertainties include limitation of *in vitro* genotoxicity assays in mimicking *in vivo* metabolism, their focusing on one or only a few types of genotoxicity events, the lack of applicability domains for ToxCast models for endocrine activity and OECD Toolbox for respiratory sensitization, limited confidence in VEGA predictions due to low ADIs and concordance indices, the limitation of OECD Toolbox in not accounting for non-immunologic mechanisms of respiratory sensitization, and the questionable reliability of chronic aquatic toxicity predictions by ECOSAR. Some of propylene carbonate'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 Propylene Carbonate

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**	**L**	DG	**L**	**L**	**L**	**M**	**L**	*L*	*L*	*M*	**H**	**L**	*L*	**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 Propylene Carbonate (CAS #108-32-7)

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

GreenScreen® Assessment (v. 1.4) Prepared By:
Name: Rachel Galante, M.P.H.
Title: Associate Toxicologist
Organization: ToxServices LLC
Date: October 12, 2018

Quality Control (v. 1.4) Performed By:
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Title: Senior Toxicologist
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Date: October 15, 2018

GreenScreen® Assessment (v.1.4) Prepared By:
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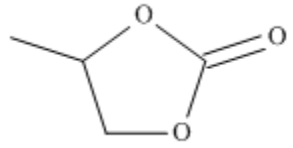
Title: Senior Toxicologist
Organization: ToxServices LLC
Date: June 16, 2021

Expiration Date: June 16, 2026[2]

Chemical Name: Propylene carbonate

CAS Number: 108-32-7

Chemical Structure(s):

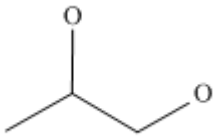


Also called: 1,3-Dioxolan-2-one, 4-methyl; 4-Methyl-1,3-dioxolan-2-one; 1,2-Propanediol carbonate; 1,2-Propanediol cyclic carbonate; 1,2-Propanediyl carbonate; 1,2-Propylene carbonate; 1-Methylethylene carbonate; 4-Methyl-2-oxo-1,3-dioxolane; 4-Methyldioxalone-2; Carbonic acid cyclic methylethylene ester; Carbonic acid, cyclic propylene ether; Carbonic acid, propylene ester; Cyclic 1,2-propylene carbonate; Cyclic methylethylene carbonate; Cyclic propylene carbonate; Dipropylene carbonate; EINECS 203-572-1; Propylene glycol cyclic carbonate (ChemIDplus 2021)

Suitable surrogates or moieties of chemicals used in this assessment (CAS #'s):
A realtively complete dataset was available for propylene carbonate; however, data gaps exist for reproductive toxicity and endocrine disruption. The ECHA REACH dossier (ECHA 2021a) identified propylene glycol (CAS #57-55-6) as a suitable read-across chemical for propylene carbonate for the reproductive toxicity endpoint. ECHA (2021a) reports that propylene carbonate is assumed to follow

[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).

the documented metabolic pathway where cyclic organic carbonates are metabolized and converted to their respective glycols; an *in vitro* hydrolysis study indicates propylene glycol is the major metabolite of propyene carbonate (ECHA 2021a), therefore, propylene glycol is considered a strong surrogate and was used to fill the data gaps.



Propylene Glycol (CAS #57-55-6)

Identify Applications/Functional Uses: (HSDB 2017)
1. Solvent and viscosity controlling agent in cosmetics
2. Electrolyte in lithium batteries
3. Natural gas purification
4. High boiling solvent in paints
5. Film-forming auxiliary
6. Auxiliary in pigment and dye industry
7. Plasticizer
8. Extraction solvent

Known Impurities[3]:
Propylene carbonate is manufactured by reacting propylene oxide and carbon dioxide in the presence of a catalyst. The reaction product is at least 99% pure; impurities consist of residual carbon dioxide and possibly some low molecular weight aldehydes and degradation products of propylene carbonate. The screen is performed on the theoretical pure substance.

GreenScreen® Summary Rating for Propylene Carbonate[4,5 6,7]: Propylene carbonate was assigned a **GreenScreen Benchmark™ Score of 3** ("Use but Still Opportunity for Improvement"). This score is based on the following hazard score combinations:

- Benchmark 3c
    - Moderate Group II Human Toxicity (skin irritation-IrS and single dose neurotoxicity-Ns)
    - High Group II Human Toxicity (eye irritation-IrE)

A data gap (DG) exists for endocrine activity-E. As outlined in GreenScreen® Guidance (CPA 2018b) Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis), propylene carbonate meets requirements for a GreenScreen Benchmark™ Score of 3 despite the hazard data gap. In a worst-case scenario, if propylene carbonate 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 Propylene Carboante

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

As previously discussed, propylene carbonate is hydrolyzed rapidly to propylene glycol in mammalian cells *in vitro*. While this reaction may also occur in the environment, as propylene carbonate is readily biodegradable (see persistence section below), no feasible and relevant environmental transformation products are expected to form.

Introduction

Propylene carbonate is a clear, colorless liquid with a weak odor. It is an important commercial chemical that is used in paints as a high-boiling solvent and film-forming auxiliary, especially in poly(vinyl fluoride) and poly(vinylidene fluoride) systems. It is also employed as an auxiliary in the pigment and dye industry and used for solvent extraction, organic synthesis, natural gas purification, as a plasticizer, and a synthetic fiber spinning solvent. It is also used in lithium batteries to decrease sulfur dioxide vapor pressure and increase electrolyte solubility and ionic conductivity. The most important and versatile method for producing carbonates is the phosgenation of hydroxy compounds; however, this method is being phased out and manufacture propylene carbonate by the catalytic insertion of carbon dioxide with oxiranes is more common. Propylene carbonate is a high production volume chemical in the United States (HSDB 2017).

ToxServices assessed propylene carbonate against GreenScreen® Version 1.4 (CPA 2018b) following procedures outlined in ToxServices' SOPs (GreenScreen® Hazard Assessment) (ToxServices 2020).

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 2020a). 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).

Propylene carbonate is listed on the U.S. EPA SCIL as a solvent with a Full Green Circle.

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 2021) 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 propylene carbonate can be found in Appendix C.

- Propylene carbonate is an LT-UNK chemical when screened using Pharos, and therefore a full GreenScreen® is required.
- Propylene carbonate is not listed on the U.S. DOT list.
- Propylene carbonate is on the following lists for multiple endpoints.
    - German FEA – Substances Hazardous to Waters: Class 1 – Low Hazard to Waters.
    - Quebec CSST – HWMIS 1998: Class D2B – Toxic material causing other toxic effects.
- Specified lists for single endpoints are reported in individual hazard endpoints in the hazard assessment section below.

Hazard Statement and Occupational Control

The following Globally Harmonized System of Classification and Labelling of Chemicals (GHS) hazard statement that was harmonized across the European Union (EU), was identified for propylene carbonate, as indicated in Table 2. General personal protective equipment (PPE) recommendations are presented in Table 3, below. No occupational exposure limits (OELs) were identified.

Table 1: GHS H Statements for Propylene Carbonate (CAS #108-32-7) (ECHA 2021a)

H Statement	H Statement Details
H319	Causes serious eye irritation

Table 2: Occupational Exposure Limits and Recommended Personal Protective Equipment for Propylene Carbonate (CAS #108-32-7)

Personal Protective Equipment (PPE)	Reference	Occupational Exposure Limits (OEL)	Reference
Eye face protection: safety glasses with side-shields	HSDB 2017	None identified	n/a
Skin protection: handle with gloves			
Body protection: impervious clothing			
Respiratory protection where appropriate			

Physicochemical Properties of Propylene Carbonate

Propylene carbonate is a clear liquid at standard temperature and pressure. It is highly soluble in water and has the potential to for a vapor based on the high vapor pressure. Its log K_{ow} of -0.41 indicates it is not likely to bioaccumulate.

Table 3: Physical and Chemical Properties of Propylene Carbonate (CAS #108-32-7)

Property	Value	Reference
Molecular formula	$C_4H_6O_3$	ChemIDplus 2021
SMILES Notation	O1[C@@H](COC1=O)C	ChemIDplus 2021
Molecular weight	102.088	ChemIDplus 2021
Physical state	Liquid	ECHA 2021a

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

Table 3: Physical and Chemical Properties of Propylene Carbonate (CAS #108-32-7)		
Property	**Value**	**Reference**
Appearance	Clear	ECHA 2021a
Melting point	-49°C	ECHA 2021a
Boiling point	242°C	ECHA 2021a
Vapor pressure	0.06 hPa at 25°C	ECHA 2021a
Water solubility	200 g/L at 25°C	ECHA 2021a
Dissociation constant	pKa = 3.92 at 20°C	ECHA 2021a
Density/specific gravity	1.21 g/cm^3 at 20°C	ECHA 2021a
Partition coefficient	Log K_{ow} = -0.41	ECHA 2021a

Toxicokinetics

An *in vitro* dermal permeability assay using human skin from the female breast reported an average permeability constant of 0.66 ± 0.44 for propylene carbonate (ECHA 2021a).

A GLP-compliant *in vitro* hydrolysis study was conducted to study the metabolism and *in vitro* degradation rate of propylene carbonate. In this study, blood freshly prepared from Wistar rats was exposed to 1 mM propylene carbonate and sampled at 0, 0.5, 1, 5, 10, and 30 minutes in order to calculate an *in vitro* half-life. The amount of hydrolysis product was quantified using liquid chromatography-mass spectrometry (LC-MS). Nearly complete hydrolysis and stoichiometric formation of propylene glycol was observed after 5 minutes, only 5.5% of the starting concentration remained, and after 30 minutes the level of the starting material was below the limit of detection. The authors concluded propylene carbonate hydrolyzes fast in the blood; the calculated half-life was 0.734 minutes which corresponds to a turnover (maximum degradation rate) of 0.68 µmol/(mL x min) (ECHA 2021a).

No *in vivo* experimental toxicokinetic studies were identified for propylene carbonate; however, ECHA has provided the following predictions (ECHA 2021a):

- An oral absorption rate of 50% is expected as propylene carbonate is a small molecule and may pass through aqueous pores or be carried through the epithelial barrier by the bulk passage of water. The water soluble liquid will readily dissolve into the gastrointestinal fluids. Additionally, its log K_{ow} value of -0.41 is favorable for absorption by passive diffusion.
- A dermal absorption rate of 50% is expected as propylene carbonate is liquid, highly water soluble and relatively small. Conversely, the substance might be too hydrophilic to cross the lipid rich environment of the stratum corneum.
- An inhalation absorption rate of 100% is proposed as worst case as a high amount is expected to be absorbed when airborne. As it is water soluble it will be readily soluble in blood.
- Wide distribution throughout the body is expected as the substance is relatively small and water-soluble. It is likely to diffuse through aqueous channels and pores. However, no bioaccumulation is expected.
- Based on the physicochemical characteristics of propylene carbonate, excretion via urine is expected, as the substance is relatively small and water soluble.
    - A toxicokinetic study using ethylene carbonate, a structural analogue to propylene carbonate, demonstrated that ethylene carbonate is primarily excreted via exhalation as carbon dioxide (57%), to a lower amount via the urine (27%) and only marginally via feces (2%).

Hazard Classification Summary

Group I Human Health Effects (Group I Human)

Carcinogenicity (C) Score (H, M, or L): L
Propylene carbonate was assigned a score of Low for carcinogenicity based on negative results in a dermal carcinogenicity study in mice. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is high as it is based on a high quality study.

- 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 2021a
  - In a GLP-compliant dermal carcinogenicity study similar to OECD Guideline 451, male C3H/HeJ mice (50/dose) were administered 50 µL undiluted propylene carbonate (purity not specified) to clipped skin twice per week for 104 weeks. Survival of the treated group was similar to controls and there were no treatment area skin tumors observed in treated mice. The incidence of tumors was not significantly different from controls. Although a squamous cell carcinoma arose in the preputial gland duct of a treated mouse, this tumor (based on its site of origin and distance from the treatment site, coupled with the lack of any evidence of preneoplastic or neoplastic change in the treatment skin of any other treated animal) was not considered to be treatment-related. Propylene carbonate was non-neoplastic in this study (Klimisch Score 2, reliable with restrictions).

Mutagenicity/Genotoxicity (M) Score (H, M, or L): *L*
Propylene carbonate was assigned a score of Low for mutagenicity/genotoxicity based on negative results for mutagenicity *in vitro* and for clastogenicity *in vivo* in high quality studies. 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 due to the initial positive results for clastogenicity in the *in vivo* micronucleus test and the lack of an additional clastogenicity test or assay to verify the negative results following the retest.

- 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 2021a
  - *In vitro:* Propylene carbonate was negative in a GLP-compliant unscheduled DNA synthesis (UDS) assay similar to OECD Guideline 482. Adult male F344 rat hepatocyte cells were exposed to propylene carbonate (purity not specified) in water at 40-4,000 µg/well without metabolic activation.[9] The positive control was 2-acetylaminofluorene. A treatment-related increase in UDS was not detected in the absence of metabolic activation. The vehicle and positive controls performed as expected (Klimisch Score 1, reliable without restriction).
  - *In vitro:* Propylene carbonate was negative in a GLP-compliant Ames bacterial reverse mutation assay conducted in a manner similar to OECD Guideline 471. *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 were exposed to propylene carbonate (purity not specified) in dimethyl sulfoxide (DMSO) at 50-5,000

[9] Hepatocytes in culture exhibit innate metabolic capacity. Therefore, the addition of exogenous metabolism is not necessary to replicate the metabolism expected in intact organisms.

µg/plate with and without metabolic activation (rat liver homogenate S9 isolated from Aroclor 1254-treated Sprague-Dawley rats). The identity of the positive control treatment(s) was not specified. No increase in the mutation frequency was identified with treatment in the presence or absence of metabolic activation. The vehicle and positive controls generated the expected results (Klimisch Score 2, reliable with restrictions).

- *In vivo:* Propylene carbonate was negative in a GLP-compliant *in vivo* micronucleus test conducted in a manner similar to OECD Guideline 474. Male and female CD-1 mice (5/sex/dose) were administered single intraperitoneal injections of propylene carbonate (purity not specified) in distilled water at 1,666 mg/kg/day and sacrificed 30, 48, or 72 hours. Femoral bone marrow samples were isolated for the micronucleus assessment. A statistically significant increase in the micronucleus incidence was detected in an initial test following sacrifice at 72 hours only; the incidence of micronuclei was 12 micronuclei/10,000 cells at 72 hours compared to 2 micronuclei/10,000 cells in the negative control and 542 micronuclei/10,000 cells for the positive control triethylenemelamine. However, the results of a re-test performed with 10 animals/sex sacrificed after 72 hours indicated no increase in the frequency of micronuclei. As the induction of micronuclei identified in the initial test occurred only at 72 hours, was of low magnitude, and was not reproducible in a retest performed with an increased number of animals, the REACH dossier authors concluded propylene carbonate was negative for micronuclei induction *in vivo* (Klimisch Score 2, reliable with restrictions).

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

Propylene carbonate was assigned a score of Low for reproductive toxicity based on no evidence of adverse effects on reproduction was identified in a two-generation reproductive toxicity study performed with the strong surrogate. GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is high as the classification is 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 2021b
  - *Surrogate: Propylene glycol (CAS #57-55-6):* A two-generation reproductive toxicity study according to the National Toxicology Program's (NTP) reproductive assessment by continuous breeding (RACB) protocol was conducted with male and female CD-1 mice (20/sex/group). The mice were provided drinking water containing the surrogate propylene glycol (purity not specified) at concentrations equivalent to 0, 1,820, 4,800, or 10,100 mg/kg/day for 7 days before mating, 98 days (14 weeks) of cohabitation, and 21 days post cohabitation. The final litters were delivered and kept for at least 21 days (weaning), and maternal animals were dosed throughout lactation. Slight increases in water consumption were measured in all parental dose groups. Body weights of parental animals and offspring were unaffected by the treatment. No treatment related effects were observed on estrous cyclicity, sperm parameters, reproductive performance, fertility, or the number, weight, or viability of the offspring. The REACH dossier authors reported a fertility and developmental NOAEL of 10,100 mg/kg based on the lack of treatment-related effects observed at up to the highest dose tested (Klimisch Score 2, reliable with restrictions).

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M, or L): L

Propylene carbonate was assigned a score of Low for developmental toxicity based on no evidence of adverse effects on development was identified in rats exposed to propylene carbonate or in mice and rats exposed to the strong surrogate propylene glycol in a developmental and reproductive toxicity study, respectively, with the exception of slight effects on ossification in rats at relatively high oral doses of propylene carbonate. Therefore, propylene carbonate does not warrant classification under GHS. GreenScreen® criteria classify chemicals as a Low hazard for developmental toxicity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is high as the classification is based on measured data for the target substance and these conclusions are supported by the lack of adverse findings in a surrogate study.

- Authoritative and Screening Lists
  - *Authoritative:* MAK – Pregnancy Risk Group C.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2021a
  - In a GLP-compliant prenatal developmental toxicity study similar to OECD Guideline 414, pregnant female Sprague-Dawley rats (27/dose) were administered gavage doses of undiluted propylene carbonate (purity not specified) at doses of 1,000, 3,000, or 5,000 mg/kg/day on gestation days 6-15. Maternal animals were examined for mortality and clinical signs, body weight, food consumption and ovary and uterine content. Fetuses were subject to external, soft tissue, skeletal, and head examinations. Mean dam body weight was significantly reduced at the high dose, and mean feed consumption was reduced in the mid and high dose dams. Clinical signs were observed in the mid and high dose groups and included immediate post-dose salivation, decreased activity, rales, abnormal gait, abnormal stance, dyspnea, piloerection, flaccid body tone, poor grooming, nasal discharge, cyanosis, and red discoloration around the mouth. Two mid dose and five high dose dams died during the study and necropsy revealed congested lungs and spongy lungs with red discoloration of the lobes. Distention of the stomach and intestines with discoloration (red/yellow) were also noted. At cesarean section, 27 (100%), 26 (96.3%), 23 (85.2%), and 22 (81.5%) animals were found gravid in the 0, 1,000, 3,000, and 5,000 mg/kg/day groups, respectively. There were no fetal malformations detected during the study. A statistically significant reduction in the number of fetuses exhibiting incomplete ossification of the 3rd sternebrae was detected in the low and mid dose group when compared to the control; however, this was considered not to be of toxicological importance by the REACH authors due to the lack of a dose response. Based on these effects, the REACH dossier authors established a maternal toxicity NOAEL of 1,000 mg/kg/day and a developmental toxicity NOAEL of ≥ 5,000 mg/kg/day for this study (Klimisch Score 2, reliable with restrictions).
- ECHA 2021b
  - *Surrogate: Propylene glycol (CAS #57-55-6):* A GLP-compliant prenatal developmental toxicity study conducted according to OECD Guideline 414 was performed with pregnant female CD-1 mice (30/dose group) administered oral gavage doses of propylene glycol (99.9% purity) at 0, 520, 5,200, or 10,400 mg/kg/day on GD 6-15. The dams were evaluated for clinical signs of toxicity, body weight, food and water consumption, and ovarian and uterine content. Fetal examinations consisted of evaluating external, visceral, skeletal, and head malformations. Decreased water consumption was measured in the mid and high dose groups. No treatment-related effects were observed on maternal health or development, and the REACH dossier authors identified a developmental NOAEL of 10,400 mg/kg/day (Klimisch Score 1, reliable without restriction).

- *Surrogate: Propylene glycol (CAS #57-55-6):* A two-generation reproductive toxicity study according to the National Toxicology Program's (NTP) reproductive assessment by continuous breeding (RACB) protocol was conducted as previously described with male and female CD-1 mice (20/sex/group). The mice were provided drinking water containing the surrogate propylene glycol (purity not specified) at concentrations equivalent to 0, 1,820, 4,800, or 10,100 mg/kg/day for 7 days before mating, 98 days (14 weeks) of cohabitation, and 21 days post cohabitation. The final litters were delivered and kept for at least 21 days (weaning), and maternal animals were dosed throughout lactation. Slight increases in water consumption were measured in all parental dose groups. Body weights of parental animals and offspring were unaffected by the treatment. No treatment related effects were observed on the number, weight, or viability of the offspring. The REACH dossier authors reported a developmental NOAEL of 10,100 mg/kg based on the lack of treatment-related effects observed at up to the highest dose tested (Klimisch Score 2, reliable with restrictions).

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

Propylene carbonate was assigned a score of Data Gap for endocrine activity based on insufficient data identified 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.
- U.S. EPA 2021
  - Propylene carbonate was active in 0/18 estrogen receptor (ER) assays, 0/14 androgen receptor (AR) assays, 0/2 steroidogenesis assays, and 0/9 thyroid receptor assays performed as part of the U.S. EPA's Endocrine Disruptor Screening Program (EDSP) in the 21st Century.
  - Propylene carbonate was predicted to be inactive for androgen receptor agonism, antagonism, and binding using the COMPARA (consensus) model in ToxCast.
- *Surrogate: Propylene Glycol (CAS #57-55-6):* Propylene glycol is listed on the TEDX - Potential Endocrine Disruptors list. The following studies are listed in the TEDX entry for propylene glycol:
  - Kassotis et al. 2015
    - The authors evaluated the endocrine-disrupting activity of chemicals used in or produced by oil and gas operations, including propylene glycol. The activity for these chemicals to interact with five nuclear receptors (estrogen, glucocorticoid, P4, thyroid, and androgen receptors) was measured, and reproductive and developmental outcomes were evaluated in male C57BL/6J mice following prenatal exposure to a mixture of these chemicals. The results indicate that 1,2-propandiol had an IC_{10} (inhibitor concentration producing 10% effect) of 27.5 µM for the estrogen receptor (ER). The study authors included propylene glycol in the glycol ethers group (ToxServices notes that 1,2-propandiol does not contain an ether functional group) and indicates that they "displayed potent activity for the estrogen and androgen receptors, with little activity exhibited for the other receptor systems." Compared to propylene glycol, the ER IC_{10} values were 0.1 µM for diethylene glycol monomethyl ether, 0.2 µM for ethylene glycol, 0.1 µM for ethylene glycol monobutyl ether, and 36.6 µM for triethylene glycol. Prenatal exposure to a mixture of 23 oil and gas operation chemicals at 3, 30, or 300 µg/kg/day produced decreased sperm counts, increased body, heart, thymus, and testes weights, and increased serum testosterone concentrations in male mice.
  - Miyoshi et al. 2001

  - Holstein cows (36 total) were administered 0 or 500 mL propylene glycol by drenching daily on lactation days 7-42. Blood samples were collected at 0, 30, and 90 minutes post-drenching once weekly during weeks 1-6 and analyzed for glucose, insulin, plasma urea nitrogen, and non-esterified fatty acids (NEFA). Blood samples were also analyzed for progesterone. Cows were palpated 3 times/week until week 11 to assess ovarian status. The propylene glycol drenching was associated with increased plasma glucose and insulin levels and decreased NEFA. The first ovulation occurred earlier in treated cows than controls (32.3 days vs. 44.5 days, p=0.06) and the length of the first luteal phase was longer in treated cows (13.1 days vs. 7.3 days, $p < 0.05$). The study authors concluded that these results "are consistent with the hypothesis that insulin is important for normal ovarian function."
- Based on a weight of evidence, a Data Gap was assigned. No data were identified for propylene carbonate. Although the surrogate propylene glycol is listed on the TEDX List, ToxServices does not consider the results of the studies listed for this chemical to be sufficient evidence for adverse effects via endocrine activity by propylene glycol. Therefore, a Data Gap was assigned.

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

Propylene carbonate was assigned a score of Low for acute toxicity based on oral and dermal LD_{50}s > 5,000 mg/kg that exceed the threshold of 2,000 mg/kg for classification under GHS criteria. GreenScreen® criteria classify chemicals as a Low hazard for acute mammalian toxicity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is high as it is based on multiple acute toxicity studies in various species.

- 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 2021a (note: only those studies reported with a Klimisch score of 1 (reliable without restriction) or 2 (reliable with restrictions) were included below)
  - *Oral*: LD_{50} (male and female Sprague-Dawley rat) > 5,000 mg/kg
  - *Oral:* LD_{50} (male and female Schmitt-Fisher and Hanover rats) = 32,319 mg/kg
  - *Dermal:* LD_{50} (male and female New Zealand white rabbit) > 2,000 mg/kg
  - *Dermal:* LD_{50} (male and female New Zealand white rabbit) > 3,000 mg/kg
- HSDB 2017
  - *Oral:* LD_{50} (rat, sex and strain not specified) = 29,100 µL/kg (35,211 mg/kg)[10]
  - *Oral:* LD_{50} (mouse, sex and strain not specified) = 20,700 mg/kg
  - *Oral:* LD_{50} (rabbit, sex and strain not specified) = 20 mL/kg (24,200 mg/kg)[11]
- ECHA 2021b
  - *Inhalation:* <u>*Surrogate: Propylene glycol (CAS #57-55-6):*</u> LC_{50} (rabbit, sex and strain not specified) > 317.041 mg/L.

[10] Based on a density of 1.21 g/cm^3 (ECHA 2021a): 29,100 µL/kg * 1 mL/1,000 µL * 1.21 g/cm^3 * 1 cm^3/1 mL * 1,000 mg/1g = 35,211 mg/kg.
[11] Based on a density of 1.21 g/cm^3 (ECHA 2021a): 20 mL/kg * 1.21 g/cm^3 * 1 cm^3/1 mL * 1,000 mg/1g = 24,200 mg/kg.

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

Propylene carbonate was assigned a score of Low for systemic toxicity (single dose) based on lack of adverse systemic effects at oral and dermal doses below 2,000 mg/kg in acute studies in rats and rabbits. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity/organ effects single exposure toxicity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is high as it is based on high quality 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 2021a (note: only those studies reported with a Klimisch score of 1 (reliable without restriction) or 2 (reliable with restrictions) were included below)
  - *Oral:* In a GLP-compliant OECD Guideline 401 acute oral toxicity study, male and female Sprague-Dawley rats (5/sex/dose) were administered propylene carbonate at a dose of 5,000 mg/kg via oral gavage and observed for 14 days. There were no mortalities and clinical signs were limited to salivation after dosing. There were no adverse changes to body weight and no visible lesions at terminal necropsy (Klimisch 1, reliable without restriction).
  - *Oral:* A non-GLP-compliant, BASF acute oral toxicity test identified an oral LD_{50} of 32,319 mg/kg in male and female Schmitt-Fisher and Hanover rats. Clinical signs of toxicity detected at 16 and 25 mL/kg included staggering, prone position, inactivity, and scrubby fur. No deaths were identified in these dose groups. At 29.1 mL/kg, all 10 animals died within 7 days; clinical signs included staggering, prone position, secretion from the stoma, and grogginess. Animals that died had spotty-reddened lungs, anemic livers, and reddened small intestines partially filled with black-red content; no abnormal gross pathological findings were reported in animals that survived to the scheduled sacrifice (Klimisch 2, reliable with restrictions).
  - *Dermal:* In a GLP-compliant OECD Guideline 402 acute dermal toxicity study, male and female New Zealand white rabbits (5/sex/dose) were administered 2,000 mg/kg undiluted propylene carbonate to clipped skin for 24 hours under occlusive conditions, and observed for 14 days. There were no mortalities reported and clinical signs were limited to the treatment site. There were no adverse changes to body weight and no visible lesions at terminal necropsy (Klimisch 1, reliable without restriction).
  - *Dermal:* In a GLP-compliant OECD Guideline 402 acute dermal toxicity study, male and female New Zealand white rabbits (5/sex/dose) were administered 3,000 mg/kg undiluted propylene carbonate to clipped skin for 24 hours under occlusive conditions, and observed for 14 days. The animals gained body weight normally during the observation period, and no gross pathological alternation were identified with treatment at necropsy (Klimisch 1, reliable without restriction).

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

Propylene carbonate was assigned a score of Low for systemic toxicity (repeated dose) based on an oral NOAEL of 3,571.4 mg/kg/day in a 90-day study in rats and an inhalation NOAEC of 0.714 mg/L in a 90-day study in rats. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (repeated dose) when oral NOAEL values are greater than 100 mg/kg/day and aerosol inhalation values are greater than 0.2 mg/L/6h/day for 90 day studies (CPA 2018b). The confidence in the score is high as it is based on high quality 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 2021a (note: only those listed with Klimisch scores of 1 (reliable without restriction) and 2 (reliable with restrictions) in the REACH dossier were included in this evaluation; range-finding studies were not included, either, as longer-duration full studies were available)
  - *Oral:* A GLP-compliant 90-day study similar to OECD Guideline 408 was conducted with male and female Sprague-Dawley rats. Animals (15/sex/dose) were administered propylene carbonate at doses of 1,000, 3,000 and 5,000 mg/kg/day via oral gavage 5 days/week for 90 days. Additional groups of the control and high dose were observed for a 28-day recovery period. Animals were observed for mortality and clinical signs, body weight, hematology and clinical chemistry; ophthalmoscopic examination, gross pathology and histopathology were performed at sacrifice. Clinical signs included alopecia, scab formation, chromodacryorrhea and dislodged upper incisors; however, authors did not consider these effects to be treatment related. Additional signs included immediate post-dose salivation, rales, abnormal gait, abnormal stance, decreased activity and dyspnea. A significant reduction in body weight and food consumption was observed in high dose males. Hematology revealed a significant decrease in mean corpuscular volume of high dose males and a significant increase in red blood cell counts, hematocrit and hemoglobin in high dose females. Mid and high dose males had significant increases in phosphorous and chloride (high dose only) values. Total bilirubin and phosphorous was significantly increased in low dose females and sodium levels were significantly increased in the high dose females. Significant decreases were noted in glucose levels in low and high dose males and females, and total protein and albumin values were decreased in high dose animals. Significant decreases were also noted in high dose male gamma-glutamyl transpeptidase (GGPT) and globulin values and high dose female calcium levels. Absolute kidney weight and relative testes weight was significantly reduced in high dose males. Gross pathological and histopathological observations were non-specific, low in incidence and without dosage-trend relationship, and therefore, considered incidental. As none of the above noted changes were dose-dependent, and there were no histomorphologic alterations attributed to test administration, the authors established the NOAEL at > 5,000 mg/kg/day for this study (Klimisch 2, reliable with restrictions).
    - The NOAEL is equal to 3,571.4 mg/kg/day when adjusted for the less than daily exposure (i.e., 5 days/7 days * 5,000 mg/kg/day = 3,571.4 mg/kg/day)
  - *Inhalation (aerosol):* A GLP-compliant 90-day study similar to OECD Guideline 413 was conducted with male and female Fisher 344 rats. Animals (15/sex/dose) were exposed to propylene carbonate aerosol via whole body inhalation at concentrations of 0, 100, 500 and 1,000 mg/m^3 6 hours/day, 5 days/week for 13 weeks. Animals were observed for mortality and clinical signs, food consumption, hematology, clinical chemistry, and urinalysis; ophthalmoscopic, gross pathological and histopathological examinations were conducted at necropsy. The only treatment related clinical sign reported was periocular swelling, however, this was also observed in the control group. No other treatment related adverse effects were reported, and the authors established the NOAEC at 1,000 mg/m^3 (1 mg/L) (Klimisch 2, reliable with restrictions).
    - The NOAEC is equal to 0.714 mg/L when adjusted for the less than daily exposure (i.e., 5 days/7 days * 1 mg/L = 0.714 mg/L).
  - *Inhalation (aerosol):* A GLP-compliant 14-day study conducted in a manner similar to OECD Guideline 412 was performed with Fisher 344/CDF rats (5/sex/group) administered whole body inhalation exposures to propylene carbonate (99% purity) aerosol at 1,000,

2,500, or 5,000 mg/m^3 (equivalent to 1, 2.5, and 5.0 mg/L, respectively) for 6 hours/day for 5 consecutive days and then for another 4 consecutive days after a 2-day break in exposure (9 total days of exposure). The equivalent concentrations for a 7-day exposure frequency were 0.71, 1.79, and 3.57 mg/L, respectively. The animals were evaluated for clinical signs of toxicity, body weight, gross pathology, organ weights, and histopathology (selected tissues). Clinical signs of toxicity included unkempt fur in the mid and high dose groups. No treatment-related mortality or effects on absolute body weight were detected, but statistically significantly reduced body weight gains were detected in males and females in all of the treatment groups. Females in the high dose group exhibited statistically significantly increased absolute and relative liver weights and relative kidney weights. The treatment-related effects on gross pathological findings were limited to increased incidence of swollen eyelids and periocular tissue in females (concentration group not specified). Histopathological evaluation indicated the swelling was due to mild subcutaneous edema. Two of five high concentration females exhibited squamous metaplasia of the maxillary and/or nasal turbinates in the nasal cavities, while one high concentration female exhibited respiratory epithelial necrosis. Additionally, one high dose male exhibited bilateral keratitis with a unilateral superficial corneal ulcer and squamous metaplasia of the arytenoid cartilages of the larynx. One female control and one male control also exhibited squamous metaplasia of the maxillary and/or nasal turbinates. The REACH dossier authors concluded that the effects on the eyes and respiratory tract resulted from irritation by the test substance. A NOAEC was not identified (Klimisch 2, reliable with restrictions).

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

Propylene carbonate was assigned a score of Low for neurotoxicity (single dose) based on evidence of transient narcotic effects following high doses of propylene carbonate and in humans and animals following high doses of the surrogate propylene glycol. GreenScreen® criteria classify chemicals as a Moderate hazard for neurotoxicity (single dose) when they are classified to GHS Category 3 (CPA 2018b). Confidence in the score is high as it is based on data from a high quality study supported by human data on 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 2021a (note: only those studies reported with a Klimisch score of 1 (reliable without restriction) or 2 (reliable with restrictions) were included below)
  - *Oral:* In the GLP-compliant OECD Guideline 401 acute oral toxicity study discussed above, male and female Sprague-Dawley rats (5/sex/dose) were administered propylene carbonate at a dose of 5,000 mg/kg via oral gavage and observed for 14 days. Clinical signs were limited to salivation after dosing (Klimisch 1, reliable without restriction).
  - *Oral:* In the acute oral toxicity study discussed above, Schmitt-Fisher and Hanover rats were administered propylene carbonate at doses of 16, 25 and 29.1 mL/kg (n=10, 4 and 10, respectively) via oral gavage. Reported clinical signs included staggering, prone position, inactivity, scrubby fur, secretion from the stoma, and grogginess at doses of ≥ 16 mL/kg (Klimisch 2, reliable with restrictions).
  - *Dermal:* In a GLP-compliant OECD Guideline 402 acute dermal toxicity study, male and female New Zealand white rabbits (5/sex/dose) were administered 2,000 mg/kg undiluted propylene carbonate to clipped skin for 24 hours under occlusive conditions, and observed for 14 days. Clinical signs were limited to the treatment site (Klimisch 1, reliable without restriction).

  - *Dermal:* In a GLP-compliant OECD Guideline 402 acute dermal toxicity study, male and female New Zealand white rabbits (5/sex/dose) were administered 3,000 mg/kg undiluted propylene carbonate to clipped skin for 24 hours under occlusive conditions, and observed for 14 days. There were no clinical signs reported (Klimisch 1, reliable without restriction).
- ATSDR 2008
  - *Surrogate: Propylene glycol (CAS #57-55-6):* In humans, the primary clinical signs of acute toxicity to propylene glycol are consequences of central nervous system (CNS) effects such as depression and lactic acid acidosis from extremely high doses following ingestion. In animals, symptoms of acute oral exposure to propylene glycol include CNS depression or narcosis.

Neurotoxicity (repeated dose, N-repeated) (Group II*) Score (H, M, or L): L
Propylene carbonate was assigned a score of Low for neurotoxicity (repeated dose) based on the lack of neurotoxic effects at concentrations up to 0.714 mg/L/day in 90-day inhalation study in rats. GreenScreen® criteria classify chemicals as a Low hazard for neurotoxicity (repeated dose) when neurotoxicity NOEAC values are greater than 0.2 mg/L/6h/day (aerosol) in inhalation studies (CPA 2018b). The confidence in the score is high as it is based on high quality 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 2021a
  - *Inhalation (aerosol):* In the previously mentioned GLP-compliant 90-day study similar to OECD Guideline 413 with male and female Fisher 344 rats, animals (15/sex/dose) were exposed to propylene carbonate via whole body inhalation at concentrations of 0, 100, 500 and 1,000 mg/m^3 6 hours/day, 5 days/week for 13 weeks. A neurobehavioral examination was conducted at 1 and 23 hours, and 6 and 13 weeks. A screen for behavioral functions was performed at 1 and 23 hours after the cessation of the first exposure. No further details on the extent or type of testing performed were provided. A functional observation battery was performed after 6 weeks and 13 weeks of exposure, and included horizontal and vertical activity, convulsions, tremors, stereotypy, piloerection, respiration, urination, gait, and acoustic startle response. The animal was then held and evaluated for pupil size, pupil response to light, vocalization, salivation, mouth breathing, lacrimation, diarrhea, visual placing, and muscle tone. Catatonia, fore and hindlimb grip strength, surface and air righting reflexes, performance on a rotating treadmill, positive geotropism (inclined screen turn), toe and tail withdrawal reflexes, hind limb splay, and rectal temperature were subsequently evaluated using simple equipment. Motor activity evaluations were also performed following 6 weeks and 13 weeks of exposure. Data for ambulatory activity, fine motor activity, rearing activity, and the sum of these activities (total activity) were collected. No significant adverse neurotoxic effects were reported (Klimisch 2, reliable with restrictions).
    - The NOAEC is equal to 0.714 mg/L when adjusted for the less than daily exposure (i.e., 5 days/7 days * 1 mg/L = 0.714 mg/L).

Skin Sensitization (SnS) (Group II*) Score (H, M, or L): *L*
Propylene carbonate was assigned a score of Low for skin sensitization based on negative modeling predictions and clinical studies in humans. GreenScreen® criteria classify chemicals as a Low hazard for skin sensitization when adequate data are available and negative and they are not GHS classified (CPA 2018). Confidence in the score is reduced as no standard tests were identified on the target substance and it is based on surrogate data and modeling predictions.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- HSDB 2017
  - Aqueous solutions of 5 and 10% propylene carbonate produced no skin irritation or sensitization in clinical studies.
  - Cosmetic products containing 0.54-20% propylene carbonate were essentially non-sensitizing to human skin.
- ECHA 2021b
  - *Surrogate: Propylene glycol (CAS #57-55-6):* A mouse local lymph node assay (equivalent or similar to OECD guideline 429) was conducted (GLP status not reported) in CBA mice at propylene glycol (purity not specified) concentrations of 50 and 100%. Stimulation indices were 1.2 and 1.6 for the two concentrations, respectively, which are below the cut-off of 3 for positive reactions. Therefore, propylene glycol is not considered a dermal sensitizer (Klimisch Score 2, reliable with restrictions).
  - *Surrogate: Propylene glycol (CAS #57-55-6):* A guinea pig maximization test (equivalent or similar to OECD guideline 406) was conducted (GLP status not reported) with female Dunkin-Hartley guinea pigs. Animals were induced dermally with undiluted propylene glycol (purity not specified) twice and challenged on day 21 with the neat substance. No positive reactions were observed in all 20 animals (Klimisch Score 2, reliable with restrictions).
  - *Surrogate: Propylene glycol (CAS #57-55-6):* A split adjuvant test (according to standard procedure of Maguire, 1973) was conducted (GLP status not reported) in female Dunkin-Hartley guinea pigs. Undiluted propylene glycol (purity not specified) did not induce any positive dermal reactions in any of the 30 animals (Klimisch Score 2, reliable with restrictions).
  - *Surrogate: Propylene glycol (CAS #57-55-6):* A non-GLP-compliant guinea pig maximization test was performed with guinea pigs (strain and sex not specified, 20 per group) induced and challenged with 70% propylene glycol (purity not specified) in water. None of the tested animals exhibited positive dermal reactions after the challenge dose (Klimisch Score 2, reliable with restrictions).
- Payne and Walsh 1994
  - Propylene carbonate does not contain any structural alerts for skin sensitization (Appendix D).
- OECD 2020a
  - Propylene carbonate does not contain any structural alerts for skin sensitization according to OECD QSAR Toolbox v4.4. Additionally, OECD QSAR Toolbox predicted that propylene carbonate is not a skin sensitizer by using the read-across method (Appendix E).
- Toxtree 2018
  - Propylene carbonate is not predicted to be a skin sensitizer using the Toxtree v3.1.0 model using decision tree methodology. This chemical has not been identified as a substrate for any of the 5 electrophilic mechanisms known to produce a skin sensitization reaction (Appendix F).
- VEGA 2021
  - Propylene carbonate is predicted to be a sensitizer using the VEGA CAESAR v2.1.6 and IRFMN/JRC v1.0.0 models. However, these predictions have low confidence as similar molecules found in the training sets have experimental values that disagree with the predicted value, a prominent number of atom centered fragments of the compound have not

been found in the compounds of the training set or are rare fragments, and the chemical is outside of the applicability domain for the models. The applicability domain index (ADI) was 0.455 and 0.544 for each of the two models, indicating that the predictions are not reliable (Appendix G).

- LabMol 2020
  - The LabMol Pred-Skin platform predicts propylene carbonate is a skin sensitizer based on the Bayesian outcome prediction with high confiability. Pred-Skin estimates confiability (or degree of confidence in the prediction) by calculating the ratio of predictions made by internal models (trees in the random forest statistical model), the applicability domain (AD), and maps for the predicted fragment contribution of the structure (Borba et al. 2021). The Bayesian outcome is based on positive predictions from DPRA, KeratinoSens, h-CLAT, LLNA and HRIPT/HMT models, with confiability scores of 92.2%, 84.1%, 60.4%, 99.3% and 96.0%, respectively. However, it may be noted propylene carbonate was outside the domain for all but one model (Appendix H).
- Based on the weight of evidence, a score of Low was assigned. Clinical studies indicate propylene carbonate is not a dermal sensitizer and available data on the surrogate propylene glycol are negative for dermal sensitizing effects. Furthermore, three of five prediction tools (Payne and Walsh, OECD Toolbox and Toxtree) provide negative results for skin sensitization. Although VEGA and LabMol provided positive results, the reliability of the predictions is low due to the compound being out of the applicability domains. Therefore, ToxServices concludes propylene carbonate is not likely to be a dermal sensitizer and a score of Low was assigned.

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

Propylene carbonate was assigned a score of Low for respiratory sensitization based on the lack of dermal sensitization potential according to ECHA's (2017) guidance. GreenScreen® criteria classify chemicals as a Low hazard for respiratory sensitization when adequate data are available and negative and they are not GHS classified (CPA 2018b). Confidence in the score is low as this evaluation does not include non-immunologic mechanisms of respiratory sensitization, which is generally based on observations in humans, 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 2020a
  - Propylene carbonate does not contain any structural alerts for respiratory sensitization (Appendix I).
- 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 propylene carbonate was not sensitizing to the skin in clinical studies and is predicted not to be a skin sensitizer (see skin sensitization section above), and a literature search did not find any human evidence of respiratory sensitization by propylene carbonate, and as propylene carbonate does not contain any structural alerts for respiratory sensitization (OECD 2020), propylene carbonate is not expected to be a respiratory sensitizer.

Skin Irritation/Corrosivity (IrS) (Group II) Score (vH, H, M, or L): *M*
Propylene carbonate was assigned a score of Moderate for skin irritation/corrosivity based on evidence of moderate skin irritation when tested undiluted in clinical studies. GreenScreen® criteria classify chemicals as a Moderate hazard for skin irritation/corrosivity when they are a mild irritant to the skin (CPA 2018b). The confidence in the score is reduced as it is based on limited human data that conflict with standard animal 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 2021a (note: only those studies reported with a Klimisch score of 1 (reliable without restriction) or 2 (reliable with restrictions) were included below)
  - Propylene carbonate was not irritating in a GLP-compliant acute dermal irritation assay similar to OECD Guideline 404. New Zealand white rabbits (3/sex) were administered topical applications of 0.5 mL undiluted propylene carbonate (purity not specified) to intact and abraded skin for 24 hours under occlusive conditions. Slight dermal irritation was observed; however, all sites returned to normal by the 72 hour observation period. The authors reported a primary dermal irritation index of 0.2 for this study. After 24 hours, the erythema scores were 0-2 (max 4) for the abraded sites and 0-1 (max 4) for the intact sites. No evidence of edema was identified following treatment. The REACH dossier authors concluded that propylene carbonate was not irritating to the skin under the conditions of this test (Klimisch 1, reliable without restriction).
  - A non-GLP-compliant acute dermal irritation assay was performed with Vienna white rabbits (n=4) administered topical applications of 0.5 g undiluted propylene carbonate (purity not specified) to shaved skin under occlusive conditions for 20 hours. After 24-72 hours, the mean erythema and edema scores were both 0, and propylene carbonate was determined to be non-irritating to the skin (Klimisch 2, reliable with restrictions).
- HSDB 2017
  - In clinical studies, undiluted propylene carbonate caused moderate skin irritation, whereas 5 and 10% propylene carbonate in aqueous solution produced no skin irritation.
- CIR 1987
  - Propylene carbonate (100%) was moderately irritating when applied to the scarified skin of 5 human volunteers for 3 days. No additional details were provided.
  - A 5% aqueous solution of propylene carbonate was not irritating to the skin of 50 human volunteers in a repeat insult patch test. No additional details were provided.
  - A 10% aqueous solution of propylene carbonate was not irritating to the skin of 50 human volunteers in a repeat insult patch test. No additional details were provided.

Eye Irritation/Corrosivity (IrE) (Group II) Score (vH, H, M, or L): H
Propylene carbonate was assigned a score of High for eye irritation/corrosivity based on is GHS classification as a Category 2A irritant in acute studies in mammals and its association with harmonized H319. GreenScreen® criteria classify chemicals as a High hazard for eye irritation/corrosivity when they are classified as a Category 2A irritant and associated with H319 (CPA 2018b). Confidence in the score is high as it is based on high quality studies and an authoritative A listing.

- Authoritative and Screening Lists
  - *Authoritative:* EU GHS – H319: Causes serious eye irritation
  - *Screening:* Japan GHS – Serious eye damage/eye irritation – Category 2A
  - *Screening:* Australia GHS – H319: Causes serious eye irritation
  - *Screening:* New Zealand GHS – 6.4A: Irritating to the eye (Category 2A)

- ECHA 2021a (note: only those studies reported with a Klimisch score of 1 (reliable without restriction) or 2 (reliable with restrictions) were included in this evaluation)
    - Propylene carbonate was irritating to the eye in a GLP-compliant acute eye irritation assay conducted according to OECD Guideline 405/EU Method B.5/EOPA OPPTS 870.2400. One eye of New Zealand white rabbits (n=3) was instilled with 0.1 mL undiluted propylene carbonate (100% purity) and observed for 10 days. Slight corneal opacity was observed in 2/3 animals for up to 2 days, slight iritis was seen in 1/3 animals for up to 1 day, and conjunctival effects (slight or moderate redness, slight or mild chemosis, and a moderate or severe discharge) were observed in all 3 animals for up to 7 days. Additional signs of irritation included Harderian or mucoid discharge, erythematous or thickened eyelids, hemorrhage of the nictitating membrane and dried secretion around the periorbital skin. The mean irritation scores for the cornea were 0, 8.3, and 3.3 at 1 hour, 1 day, and 2 days, respectively. The mean irritation scores for the iris were 0 and 1.7 at 1 hour and 1 day, respectively. The mean irritation scores for the conjunctiva were 13.3, 13.3, 10, 4.7, 3.3, and 1 at 1 hour, 1 day, 2 days, 3 days, 4 days, and 7 days, respectively. The maximum mean total score (MMTS) on day one was 23.3/110, and the mean final irritation score on day seven was 5/8. The summary did not report on evaluations beyond day 7, but stated that effects were fully reversible within 10 days. Based on these results, the REACH dossier authors classified propylene carbonate as a Category 2A irritant (Klimisch 1, reliable without restriction).
    - A GLP-compliant hen's egg-chorioallantoic membrane test (HET-CAM) was performed with hen's eggs (1-4/group) exposed to 0.3 mL propylene carbonate (purity not specified) in Pluronic PE 6200 or in doubly distilled water at 10%, 20%, 40%, 60%, 80%, or 100% for up to 3.5 minutes. According to REACH dossier authors, the threshold concentration for effects indicating serious eye damage was > 10% and < 20%, and the EC90 for propylene carbonate was identified as 17% (Klimisch Score 1, reliable without restriction). Therefore, the REACH dossier authors concluded that propylene carbonate may cause irreversible effects on the eye (Klimisch 1, reliable without restriction).
    - Propylene carbonate was irritating to the eye in a GLP-compliant acute eye irritation assay conducted according to OECD Guideline 405/EU Method B.5/EPA OPPTS 870.2400. One eye of New Zealand white rabbits (n=3) was instilled with 0.1 mL undiluted propylene carbonate (99.9% purity) and observed for 7 days. Slight to mild corneal opacity was observed in 3/3 animals for up to 4 days, slight iritis was seen in 2/3 animals for up to 4 days, and conjunctival effects (slight or moderate redness, slight or mild chemosis, and slight to severe discharge) were observed in all 3 animals for up to 5 days. Additional signs of irritation included Harderian or mucoid discharge, thickened, erythematous or convoluted eyelids, hemorrhage of the nictitating membrane, and dried secretion around the periorbital skin and irregular corneal surface. The mean irritation scores at 1 hour, 1 day, 2 days, 3 days, and 4 days were $\underline{\geq}$13.3, $\underline{\geq}$16.7, $\underline{\geq}$20, $\underline{\geq}$20, and $\underline{\geq}$20, respectively, for the cornea, $\underline{\geq}$0, $\underline{\geq}$3.3, $\underline{\geq}$3.3, $\underline{\geq\geq}$3.3, and $\underline{\geq}$3.3, respectively, for the iris, and $\underline{\geq}$13.3, $\underline{\geq}$14, $\underline{\geq}$9.3, $\underline{\geq}$6, and $\underline{\geq}$5.3, respectively, for the conjunctiva.[12] The maximum mean total score (MMTS) on day one was 34/110, and the mean final irritation score on day seven was 5/8. Based on these results, the REACH dossier authors classified propylene carbonate as a Category 2A irritant (Klimisch 1, reliable without restriction).
    - Propylene carbonate was not irritating to the eye in a GLP-compliant acute eye irritation assay conducted similar to OECD Guideline 405. One eye of New Zealand white rabbits (n=6) was instilled with 0.1 mL undiluted propylene carbonate (purity not specified) and

[12] << is the symbol presented in the REACH dossier; however, ToxServices believes that the symbol should be "≤".

observed for 7 days. The maximum mean total scores were 12.5, 9.8, 5.1, 4.8, and 0 (max 110) at 1, 24, 48, 72 hours, and 7 days, respectively. No further details were provided. The REACH dossier authors concluded propylene carbonate was not irritating under the conditions of this study (Klimisch 1, reliable without restriction).

Ecotoxicity (Ecotox)

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

Propylene carbonate was assigned a score of Low for acute aquatic toxicity based on L/EC_{50} values of > 100 mg/L in all three trophic levels. GreenScreen® criteria classify chemicals as a Low hazard for acute aquatic toxicity when acute aquatic toxicity values are greater than 100 mg/L (CPA 2018b). The confidence in the score is high as it is based on high quality measured data for all three trophic levels.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2021a
  - 96hr LC_{50} (*Cyprinus carpio*, carp) >1,000 mg/L (Klimisch 1, reliable without restriction)
  - 48hr EC_{50} (*Daphnia magna*, daphnia) > 1,000 mg/L (Klimisch 1, reliable without restriction)
  - 72hr EC_{50} (*Desmodesmus subspicatus*, green algae) > 900 mg/L (biomass and growth rate) (Klimisch 2, reliable with restrictions)
  - 72hr EC_{50} (*Selenastrum* sp., green algae) > 929 mg/L (growth rate) (Klimisch 1, reliable without restriction)

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

Propylene carbonate was assigned a score of Low for chronic aquatic toxicity based on modeled and experimental chronic aquatic toxicity values of >10 mg/L in all three trophic levels. GreenScreen® criteria classify chemicals as a Low hazard for chronic aquatic toxicity when chronic aquatic toxicity values are >10 mg/L (CPA 2018b). Confidence in the score is reduced as it is based on modeled data for two trophic levels.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2021a
  - 72hr NOEC (*Desmodesmus subspicatus*, green algae) = 900 mg/L (Klimisch 2, reliable with restrictions)
  - 72hr NOEC (*Selenastrum* sp., green algae) = 929 mg/L (growth rate) (Klimisch 1, reliable without restriction)
- U.S. EPA 2017a
  - Propylene carbonate was assigned to the esters ECOSAR chemical class. The most conservative ChV values are 43.51 mg/L in fish, 1,283.22 mg/L in daphnia and 68.58 mg/L in green algae (Appendix J).

Environmental Fate (Fate)

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

Propylene carbonate was assigned a score of Very Low for persistence based on it being readily biodegradable and meeting the 10-day window in two biodegradation studies. GreenScreen® criteria classify chemicals as a Very Low hazard for persistence when they are readily biodegradable and meet

the 10-day window when they mainly partition to soil, water or sediment (CPA 2018b). The confidence in the score is high as it is based on high quality 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 2021a (note: only those listed with a Klimisch score of 1 (reliable without restriction) or 2 (reliable with restrictions) were included in this evaluation)
    - Propylene carbonate was readily biodegradable and met the 10-day window in a GLP-compliant OECD Guideline 301B (CO_2 Evolution) test. In this assay, aerobic activated sludge (adaption not specified) was exposed to propylene carbonate (100% purity) at 20 mg/L for 29 days in two replicates. Propylene carbonate degraded 70.2% and 69.3% in 9 days and 87.7% and 83.5% in 29 days (Klimisch 1, reliable without restriction).
    - Propylene carbonate was readily biodegradable and met the 10-day window in a GLP-compliant EU Method C.4-A (DOC Die-Away) test. In this assay, anaerobic activated sludge (adaption not specified) was exposed to propylene carbonate (99.9% purity) at 14 mg/L for 14 days. Propylene carbonate degraded 97% in 14 days. No specific details were provided regarding the degree of degradation reached within the 10-day window (Klimisch 1, reliable without restriction).
- U.S. EPA 2017b
    - The BIOWIN model of EPI Suite™ predicts that propylene carbonate is not readily biodegradable. Level III fugacity modeling (MCI method) indicates 64.3% will partition to soil with a half life of 720 hours (30 days), 34.9% to water with a half life of 360 hours (15 days), and 0.662% to air with a half life of 67.8 hours (Appendix K).

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

Propylene carbonate was assigned a score of Very Low for bioaccumulation based on a log K_{ow} of -0.41 and a predicted BCF of 0.9145. GreenScreen® criteria classify chemicals as a Very Low hazard for bioaccumulation when their log K_{ow} is ≤ 4 and their BCF value is ≤ 100 (CPA 2018b). Confidence is high as it is based in part 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.
- U.S. EPA 2017b
    - BCFBAF predicts a BCF of 3.162 L/kg wet-wt using the regression based model based on a measured log K_{ow} of -0.41, and a BCF of 0.9145 using the Arnot-Gobas model for the upper trophic level, taking metabolism into consideration. Propylene carbonate is within the applicability domain of both models in BCFBAF (Appendix K).

Physical Hazards (Physical)

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

Propylene carbonate was assigned a score of Low for reactivity based on its structure indicating it is non-oxidizing and non-explosive. GreenScreen® criteria classify chemicals as a Low hazard for reactivity when they are not explosive or self-reactive (CPA 2018b). The confidence in the score was reduced due to lack of 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 2021a
    - Based on its chemical structure, propylene carbonate is non-oxidizing. The oxygen molecules in propylene carbonate are only chemically bound to carbon molecules. Furthermore, the substance does not contain any chemical groups associated with oxidizing properties and is therefore considered not to be oxidizing.
    - Based on its chemical structure, propylene carbonate is non-explosive. Propylene carbonate is considered not to contain any chemical groups indicating explosive properties and is therefore considered not to be explosive.

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

Propylene carbonate was assigned a score of Low for flammability based on its flash point of 116°C. GreenScreen® criteria classify chemicals as a Low hazard for flammability when adequate data are available and they are not GHS classified (i.e., having a flash point of >93ºC as a liquid) (CPA 2018b). The confidence in the score was high as it is 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 2021a
    - Propylene carbonate had flash point of 135°C in a closed cup assay and an open cup assay.
    - Propylene carbonate had flash point of 116°C in a DIN 51758 closed cup assay.
    - Based on its chemical structure, propylene carbonate is not flammable in contact with water and air and also not pyrophoric. In the daily use and handling of propylene carbonate during which continuous exposure to air can occur, no spontaneous ignition is observed. The absence of structural alerts furthermore confirms that it is highly unlikely that propylene carbonate has pyrophoric properties. The absence of structural alerts also indicates that it is highly unlikely that propylene carbonate is flammable in contact with water, which is confirmed by the observations that in handling the substance in contact with water no flammable properties are observed.

Use of New Approach Methodologies (NAMs)[13] in the Assessment, Including Uncertainty Analyses of Input and Output

New Approach Methodologies (NAMs) used in this GreenScreen® include *in silico* modeling for endocrine activity, skin sensitization, respiratory sensitization, chronic aquatic toxicity, and bioaccumulation, and *in vitro* assays for mutagenicity and endocrine activity. NAMs are non-animal alternative 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 2020b, OECD 2020b). 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 2020b):

- 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 propylene carbonate's NAMs dataset include no or lack of adequate experimental or human data for endocrine activity, skin sensitization, respiratory sensitization, and chronic aquatic toxicity. Propylene carbonate's Type II (extrapolation output) uncertainties include limitation of *in vitro* genotoxicity assays in mimicking *in vivo* metabolism, their focusing on one or only a few types of genotoxicity events, the lack of applicability domains for ToxCast models for endocrine activity and OECD Toolbox for respiratory sensitization, limited confidence in VEGA predictions due to low ADIs and concordance indices, the limitation of OECD Toolbox in not accounting for non-immunologic mechanisms of respiratory sensitization, and the questionable reliability of chronic aquatic toxicity predictions by ECOSAR. Some of propylene carbonate'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 2020b)	
Type I Uncertainty: Data/Model Input	**Endocrine activity:** No *in vivo* experimental data are available. **Skin sensitization**: No high quality experimental data are available on the target substance. Some *in vivo* data available on propylene glycol surrogate. **Respiratory sensitization**: No experimental data are available and there are no validated test methods. **Chronic aquatic toxicity**: No experimental data are available for two trophic levels.
Type II Uncertainty: Extrapolation Output	**Genotoxicity:** The bacterial reverse mutation assay (as defined in OECD Guideline 471) only tests point-mutation inducing activity in

[13] 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).

	non-mammalian cells, and the exogenous metabolic activation system does not entirely mimic *in vivo* conditions[14]. The *in vitro* UDS assay detects "longpatch repair" but is less sensitive for detection of "shortpatch repair". Mutagenic events may result from non-repair, misrepair, or misreplication of DNA lesions, and UDS gives no indication of fidelity of the repair process. It is possible that a mutagen interacts with DNA but damage is not repaired by an excision repair process.[15] **Endocrine activity:** ToxCast models do not define applicability domain; the *in vivo* relevance of EDSP Tox 21 screening assays is unknown due to lack of consideration of metabolism and other toxicokinetic factors. **Skin sensitization:** Payne and Walsh (1994) and Toxtree only identify structural alerts, and no applicability domain can be defined (Toxtree 2018). No reliable predictions were produced in VEGA (VEGA 2021). Although the Bayesian outcome prediction in LabMol had high confiability, the target substance was out of the domain for all but one individual model. **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. **Chronic aquatic toxicity**: The reliability of predicted chronic aquatic toxicity is questionable as the predicted acute values are more conservative than the measured acute values.	
Endpoint	**NAMs Data Available and Evaluated? (Y/N)**	**Types of NAMs Data (*in silico* modeling/*in vitro* biological profiling/frameworks)**
Carcinogenicity	N	
Mutagenicity	Y	*In vitro* data: Bacterial reverse mutation assay/ *in vitro* UDS assay
Reproductive toxicity	N	
Developmental toxicity	N	
Endocrine activity	Y	*In vitro* high throughput data: EDSP Tox 21 screening assays/ *in silico* modeling*:* ToxCast models
Acute mammalian toxicity	N	
Single exposure systemic toxicity	N	
Repeated exposure systemic toxicity	N	
Single exposure neurotoxicity	N	

[14] https://www.oecd-ilibrary.org/docserver/9789264071247-en.pdf?expires=1614097593&id=id&accname=guest&checksum=89925F80B9F4BD2FFC6E90F94A0EE427
[15] https://www.oecd-ilibrary.org/environment/test-no-486-unscheduled-dna-synthesis-uds-test-with-mammalian-liver-cells-in-vivo_9789264071520-en#:~:text=The%20purpose%20of%20the%20unscheduled,physical%20agents%20in%20the%20liver.

Repeated exposure neurotoxicity	N	
Skin sensitization	Y	*In silico* modeling: VEGA/Payne and Walsh (1994) structural alerts/ Toxtree/OECD Toolbox/LabMol
Respiratory sensitization	Y	*In silico* modeling: OECD Toolbox structural alerts
Skin irritation	N	
Eye irritation	N	
Acute aquatic toxicity	N	
Chronic aquatic toxicity	Y	*In silico* modeling: ECOSAR
Persistence	Y	*In silico* modeling: EPI Suite™ Non-animal testing: OECD Guideline 301B (CO_2 Evolution) test; EU Method C.4-A (DOC Die-Away) test
Bioaccumulation	Y	*In silico* modeling: EPI Suite™

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APPENDIX A: Hazard Classification Acronyms
(in alphabetical order)

(AA) Acute Aquatic Toxicity

(AT) Acute Mammalian Toxicity

(B) Bioaccumulation

(C) Carcinogenicity

(CA) Chronic Aquatic Toxicity

(D) Developmental Toxicity

(E) Endocrine Activity

(F) Flammability

(IrE) Eye Irritation/Corrosivity

(IrS) Skin Irritation/Corrosivity

(M) Mutagenicity and Genotoxicity

(N) Neurotoxicity

(P) Persistence

(R) Reproductive Toxicity

(Rx) Reactivity

(SnS) Sensitization- Skin

(SnR) Sensitization- Respiratory

(ST) Systemic/Organ Toxicity

APPENDIX B: Results of Automated GreenScreen® Score Calculation for Propylene Carbonate (CAS #108-32-7)

TOXSERVICES TOXICOLOGY RISK ASSESSMENT CONSULTING

GREEN SCREEN FOR SAFER CHEMICALS

GreenScreen® Score Inspector

Table 1: Hazard Table

			Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
			Carcinogenicity	Mutagenicity/Genotoxicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
Table 2: Chemical Details									S	R *	S	R *	*	*								
Inorganic Chemical?	**Chemical Name**	**CAS#**	**C**	**M**	**R**	**D**	**E**	**AT**	**STs**	**STr**	**Ns**	**Nr**	**SNS***	**SNR***	**IrS**	**IrE**	**AA**	**CA**	**P**	**B**	**Rx**	**F**
No	Propylene Carbonate	108-32-7	L	*L*	L	L	DG	L	L	L	M	L	*L*	*L*	*M*	H	L	*L*	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	No	No	No
3	No	No	Yes	No			
4	STOP						

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
Propylene Carbonate	3

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

Table 6

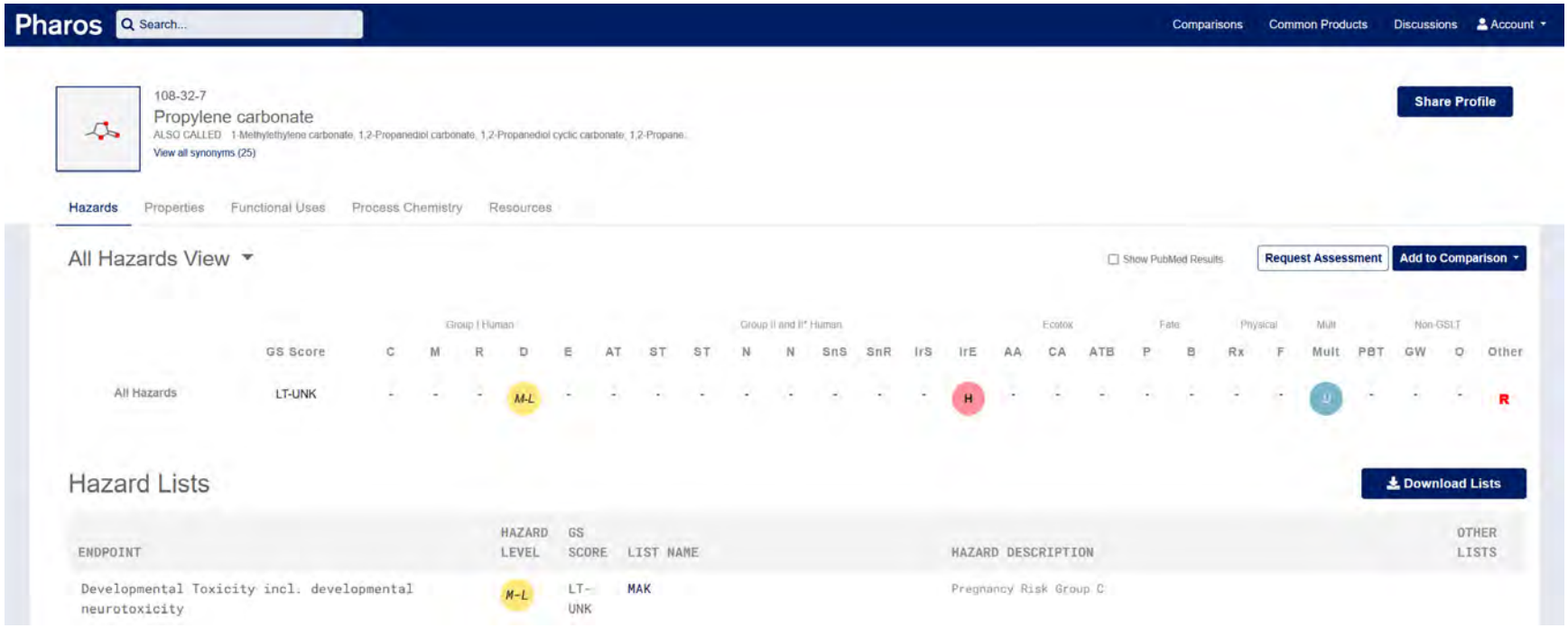
Chemical Name	Final GreenScreen® Benchmark Score
Propylene Carbonate	3

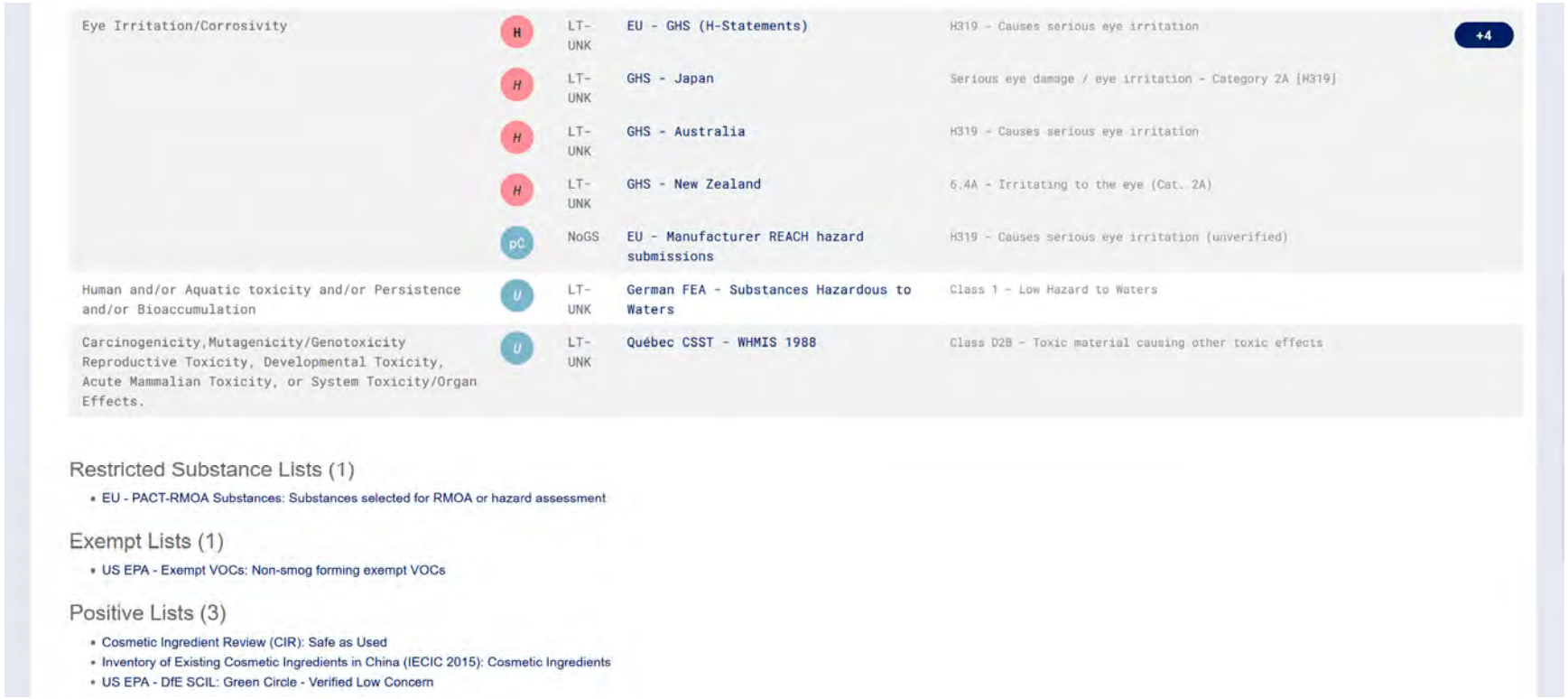
After Data gap Assessment
Note: No Data gap Assessment Done if Preliminary GS Benchmark Score is 1.

Table 5: Data Gap Assessment Table

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

APPENDIX C: Pharos Output for Propylene Carbonate (CAS #108-32-7)

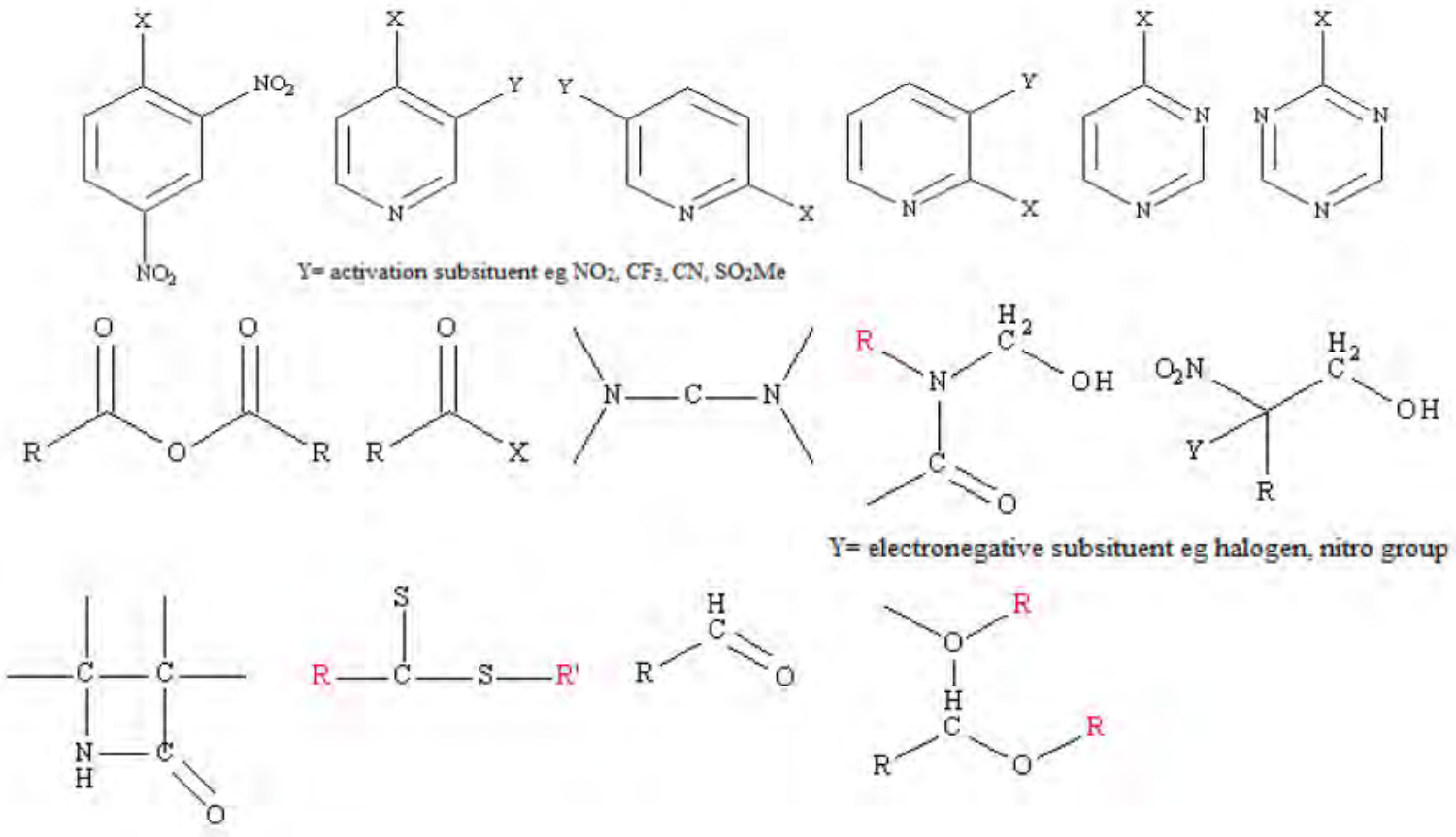


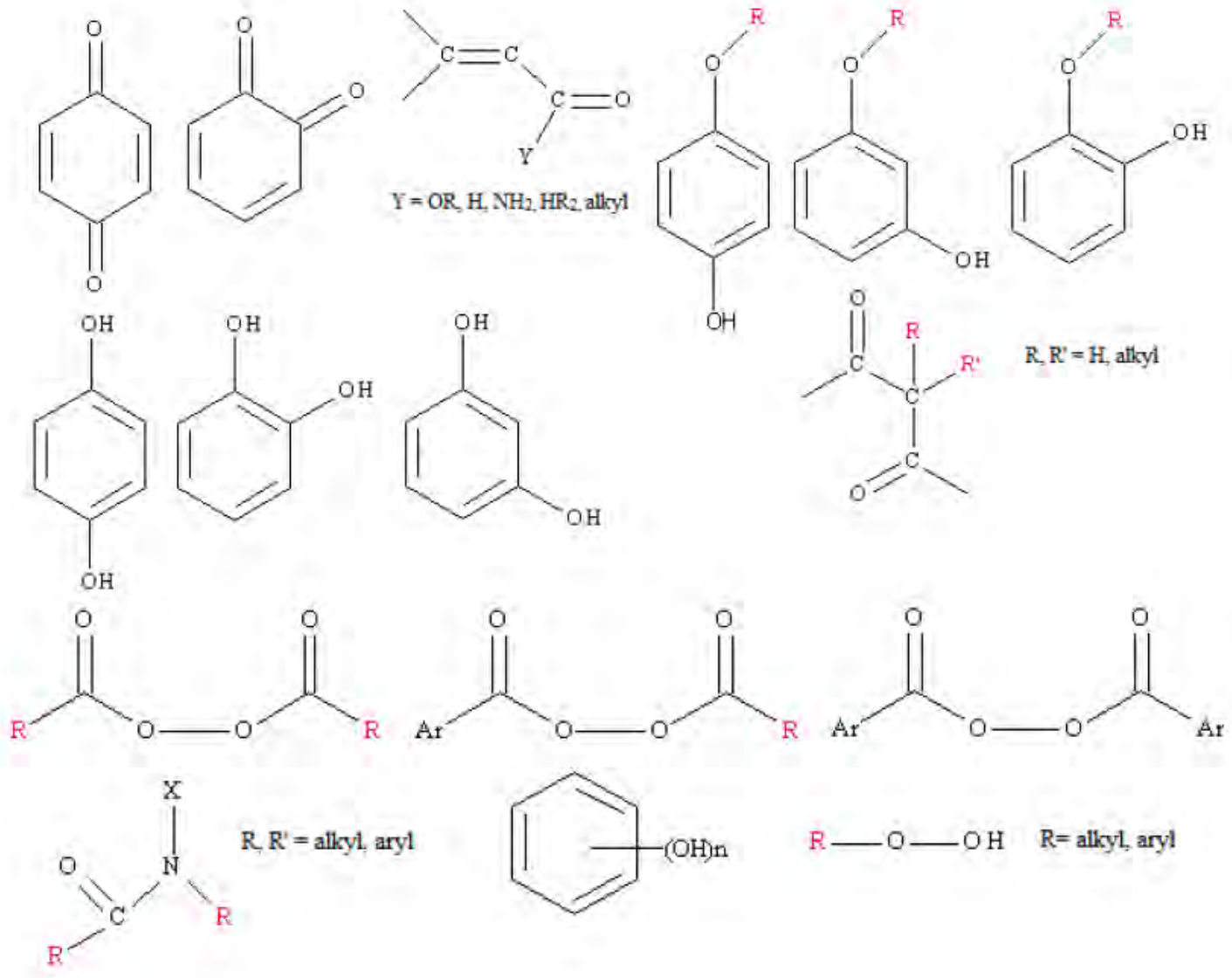


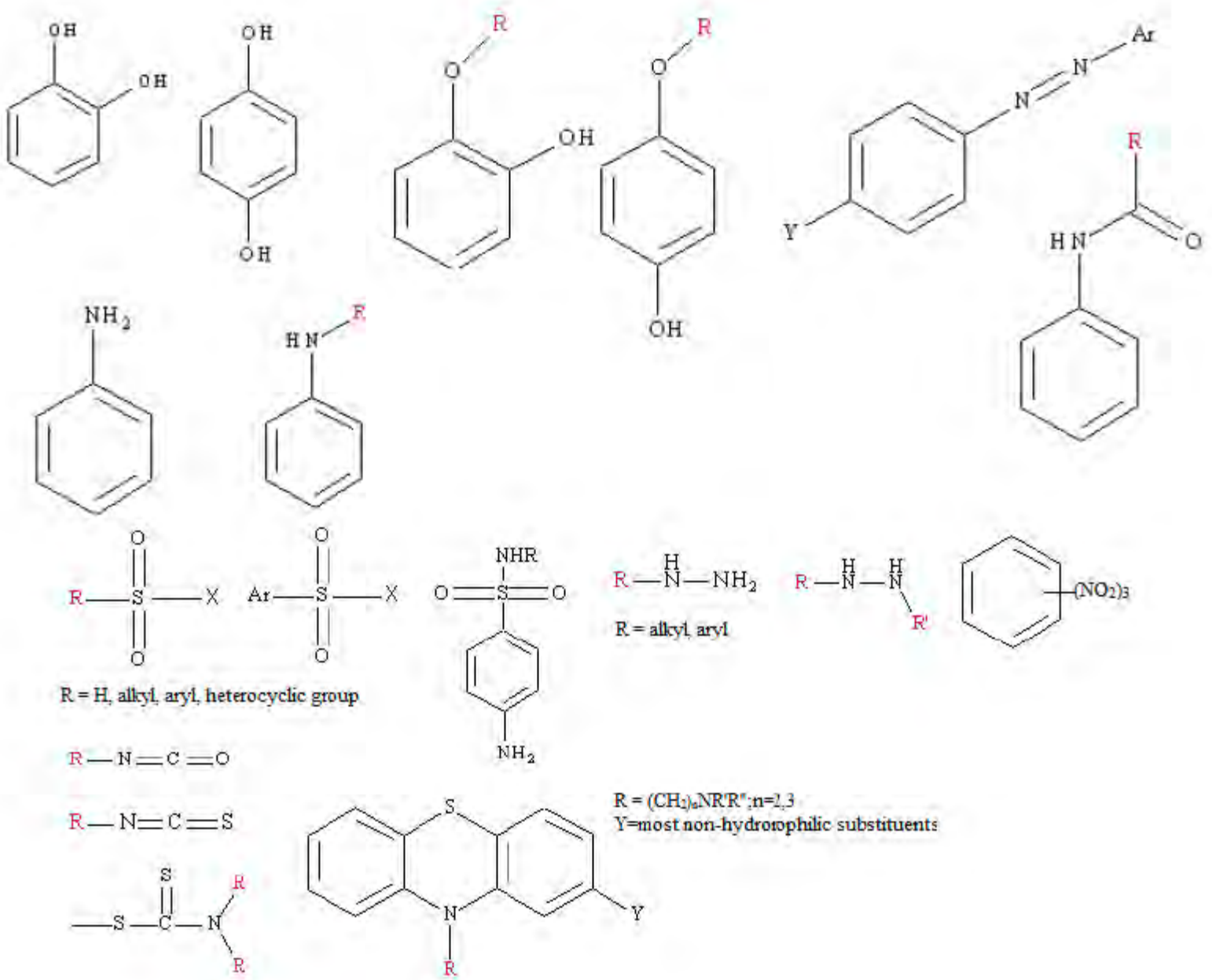
Eye Irritation/Corrosivity	H	LT-UNK	EU - GHS (H-Statements)	H319 - Causes serious eye irritation	+4
	H	LT-UNK	GHS - Japan	Serious eye damage / eye irritation - Category 2A [H319]	
	H	LT-UNK	GHS - Australia	H319 - Causes serious eye irritation	
	H	LT-UNK	GHS - New Zealand	6.4A - Irritating to the eye (Cat. 2A)	
	pC	NoGS	EU - Manufacturer REACH hazard submissions	H319 - Causes serious eye irritation (unverified)	
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	
Carcinogenicity,Mutagenicity/Genotoxicity Reproductive Toxicity, Developmental Toxicity, Acute Mammalian Toxicity, or System Toxicity/Organ Effects.	U	LT-UNK	Québec CSST - WHMIS 1988	Class D2B - Toxic material causing other toxic effects	

APPENDIX D: Known Structural Alerts for Skin Sensitization

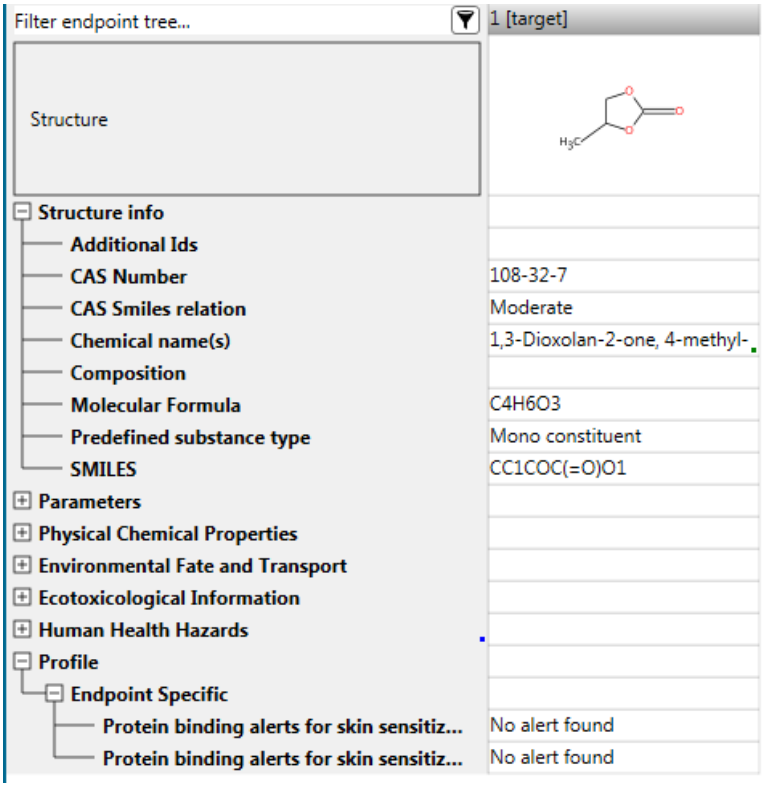
Below are known structural alerts for skin sensitizers (Payne and Walsh 1994). Propylene carbonate does not possess any structural alerts for skin sensitization.





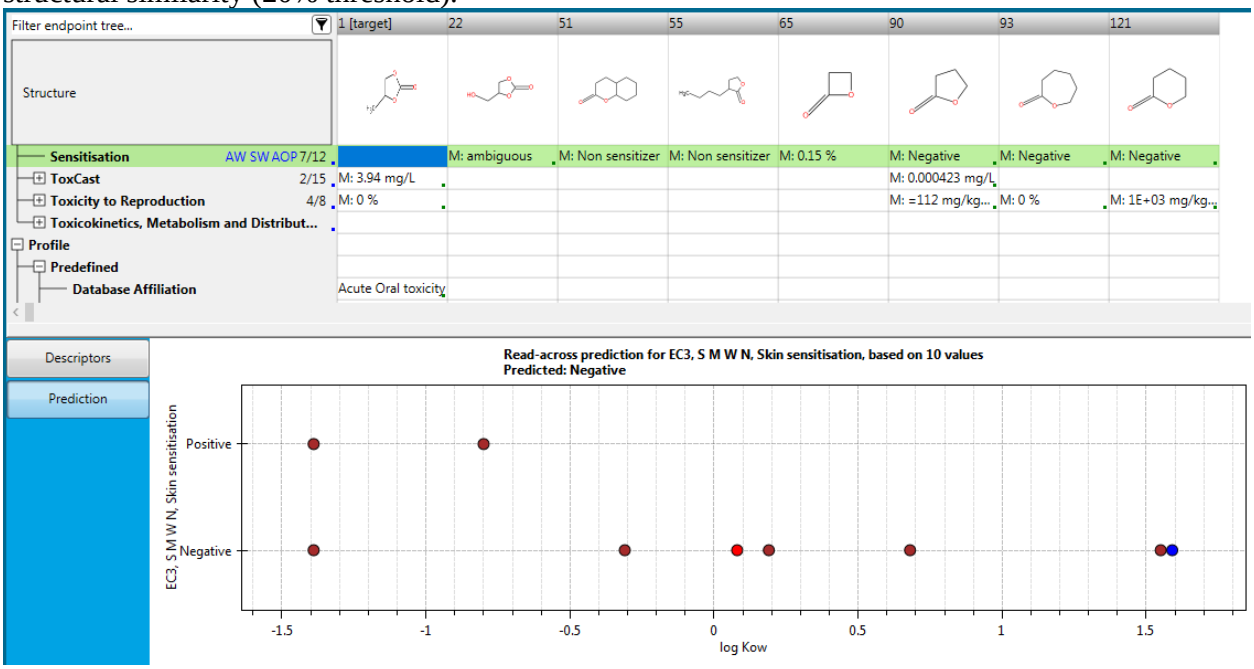


APPENDIX E: OECD Toolbox Skin Sensitization Results for Propylene Carbonate (CAS #108-32-7)



Filter endpoint tree...	1 [target]
Structure	
Structure info	
Additional Ids	
CAS Number	108-32-7
CAS Smiles relation	Moderate
Chemical name(s)	1,3-Dioxolan-2-one, 4-methyl-
Composition	
Molecular Formula	C4H6O3
Predefined substance type	Mono constituent
SMILES	CC1COC(=O)O1
Parameters	
Physical Chemical Properties	
Environmental Fate and Transport	
Ecotoxicological Information	
Human Health Hazards	
Profile	
Endpoint Specific	
Protein binding alerts for skin sensitiz...	No alert found
Protein binding alerts for skin sensitiz...	No alert found

Read across chemicals were categorized by Oncologic Primary Classification and subcategorized by structural similarity (20% threshold).



Filter endpoint tree...	1 [target]	22	51	55	65	90	93	121
Structure								
Sensitisation AW SW AOP 7/12		M: ambiguous	M: Non sensitizer	M: Non sensitizer	M: 0.15 %	M: Negative	M: Negative	M: Negative
ToxCast 2/15	M: 3.94 mg/L					M: 0.000423 mg/L		
Toxicity to Reproduction 4/8	M: 0 %					M: =112 mg/kg...	M: 0 %	M: 1E+03 mg/kg...
Toxicokinetics, Metabolism and Distribut...								
Profile								
Predefined								
Database Affiliation	Acute Oral toxicity							

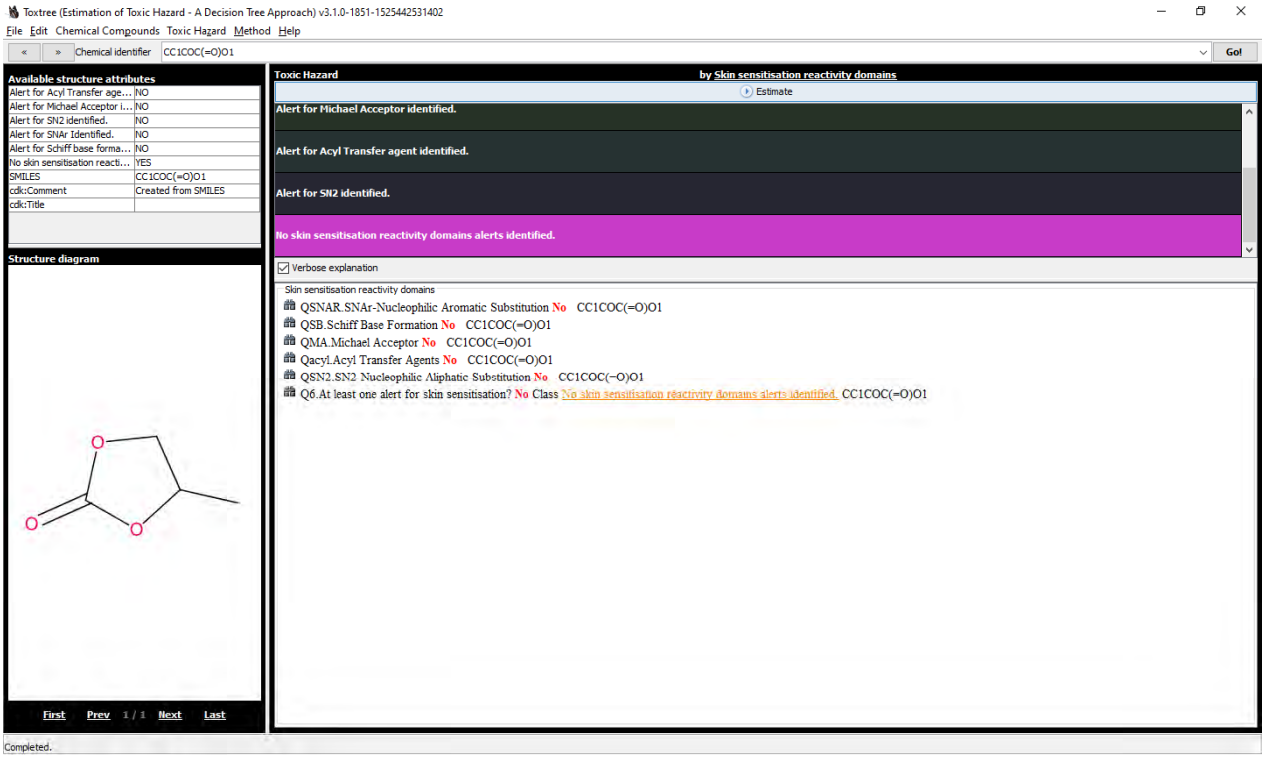
Descriptors
Prediction

Read-across prediction for EC3, S M W N, Skin sensitisation, based on 10 values
Predicted: Negative

EC3, S M W N, Skin sensitisation: Positive, Negative

-1.5 -1 -0.5 0 0.5 1 1.5
log Kow

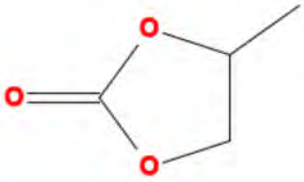
APPENDIX F: Toxtree Skin Sensitization Results for Propylene Carbonate (CAS #108-32-7)



APPENDIX G: VEGA Skin Sensitization Results for Propylene Carbonate (CAS #108-32-7)

1. Prediction Summary

Prediction for compound Molecule 0

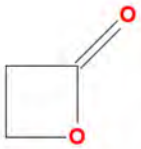


Prediction: Reliability:

Prediction is Sensitizer, 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
- a prominent number of atom centered fragments of the compound have not been found in the compounds of the training set or are rare fragments (1 unknown fragments found)

Compound: Molecule 0
Compound SMILES: O=C1OCC(O1)C
Experimental value: -
Predicted skin sensitization activity: Sensitizer
O(Active): 1
O(Inactive): 0
Reliability: the predicted compound is outside the Applicability Domain of the model
Remarks:
none

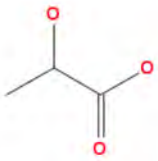
3.1 Applicability Domain:
Similar Compounds, with Predicted and Experimental Values



Compound #1

CAS: 57-57-8
Dataset id: 183 (Training set)
SMILES: O=C1OCC1
Similarity: 0.819

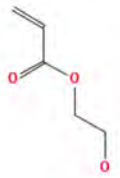
Experimental value: Sensitizer
Predicted value: Sensitizer



Compound #2

CAS: 50-21-5
Dataset id: 127 (Training set)
SMILES: O=C(O)C(O)C
Similarity: 0.799

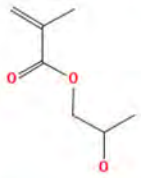
Experimental value: NON-Sensitizer
Predicted value: NON-Sensitizer



Compound #3

CAS: 818-61-1
Dataset id: 110 (Training set)
SMILES: O=C(OCCO)C=C
Similarity: 0.768

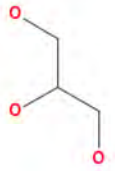
Experimental value: Sensitizer
Predicted value: Sensitizer



Compound #4

CAS: 923-26-2
Dataset id: 112 (Test set)
SMILES: O=C(OCC(O)C)C(=C)C
Similarity: 0.765

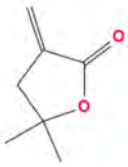
Experimental value: NON-Sensitizer
Predicted value: Sensitizer



Compound #5

CAS: 56-81-5
Dataset id: 102 (Test set)
SMILES: OCC(O)CO
Similarity: 0.756

Experimental value: NON-Sensitizer
Predicted value: NON-Sensitizer



Compound #6

CAS: 29043-97-8
Dataset id: 81 (Test set)
SMILES: O=C1OC(C)(C)CC1(=C)
Similarity: 0.738

Experimental value: Sensitizer
Predicted value: Sensitizer

3.2 Applicability Domain:
Measured Applicability Domain Scores

Global AD Index
AD index = 0.455
Explanation: the predicted compound is outside the Applicability Domain of the model.

Similar molecules with known experimental value
Similarity index = 0.809
Explanation: strongly similar compounds with known experimental value in the training set have been found.

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 = 0.508
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 = 0.6
Explanation: a prominent number of atom centered fragments of the compound have not been found in the compounds of the training set or are rare fragments (1 unknown fragments found).

Symbols explanation:

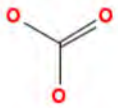
The feature has a good assessment, model is reliable regarding this aspect.

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.

4.1 Reasoning:
Relevant Chemical Fragments and Moieties

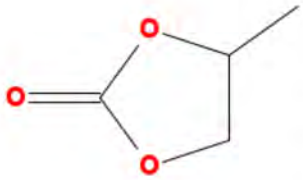
(Molecule 0) Reasoning on rare and missing Atom Centered Fragments.
The following Atom Centered Fragments have been found in the molecule, but they are not found or rarely found in the model's training set:



Fragment defined by the SMILES: O=C(O)O
The fragment has never been found in the model's training set

1. Prediction Summary

Prediction for compound Molecule 0

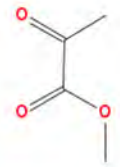


Prediction: Reliability:

Prediction is Sensitizer, 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:
- a prominent number of atom centered fragments of the compound have not been found in the compounds of the training set or are rare fragments (1 unknown fragments found)

Compound: Molecule 0
Compound SMILES: O=C1OCC(O1)C
Experimental value: -
Predicted skin sensitization activity: Sensitizer
Reliability: the predicted compound is outside the Applicability Domain of the model
Remarks:
none

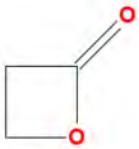
3.1 Applicability Domain:
Similar Compounds, with Predicted and Experimental Values



Compound #1

CAS: 600-22-6
Dataset id: 165 (Training set)
SMILES: O=C(OC)C(=O)C
Similarity: 0.825

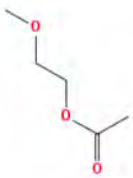
Experimental value: Sensitizer
Predicted value: Sensitizer



Compound #2

CAS: 57-57-8
Dataset id: 284 (Test set)
SMILES: O=C1OCC1
Similarity: 0.819

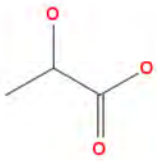
Experimental value: Sensitizer
Predicted value: Sensitizer



Compound #3

CAS: 110-49-6
Dataset id: 322 (Test set)
SMILES: O=C(OCCOC)C
Similarity: 0.818

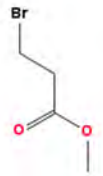
Experimental value: NON-Sensitizer
Predicted value: NON-Sensitizer



Compound #4

CAS: 50-21-5
Dataset id: 197 (Training set)
SMILES: O=C(O)C(O)C
Similarity: 0.799

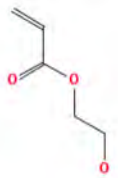
Experimental value: NON-Sensitizer
Predicted value: Sensitizer



Compound #5

CAS: 3395-91-3
Dataset id: 250 (Training set)
SMILES: O=C(OC)CCBr
Similarity: 0.787

Experimental value: NON-Sensitizer
Predicted value: NON-Sensitizer



Compound #6

CAS: 818-61-1
Dataset id: 44 (Training set)
SMILES: O=C(OCCO)C=C
Similarity: 0.768

Experimental value: Sensitizer
Predicted value: Sensitizer

3.2 Applicability Domain:
Measured Applicability Domain Scores

Global AD Index
AD index = 0.544
Explanation: the predicted compound is outside the Applicability Domain of the model.

Similar molecules with known experimental value
Similarity index = 0.822
Explanation: strongly similar compounds with known experimental value in the training set have been found.

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 = 0.6
Explanation: a prominent number of atom centered fragments of the compound have not been found in the compounds of the training set or are rare fragments (1 unknown fragments found).

Symbols explanation:

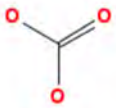
The feature has a good assessment, model is reliable regarding this aspect.

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.

4.1 Reasoning:
Relevant Chemical Fragments and Moieties

(Molecule 0) Reasoning on rare and missing Atom Centered Fragments.
The following Atom Centered Fragments have been found in the molecule, but they are not found or rarely found in the model's training set:



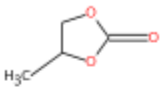
Fragment defined by the SMILES: O=C(O)O
The fragment has never been found in the model's training set

APPENDIX H: LabMol Skin Sensitization Results for Propylene Carbonate (CAS #108-32-7)

Chemical Exposure	Molecular initiating event *in chemico*	Cellular response *in vitro*		Tissue / Organ response *in vivo*	Organism response *in vivo*	Pred-Skin 3.0 Outcome *in silico*
•Skin Penetration •Electrophilic substance: directly or via auto-oxidation or metabolism	Covalent interaction with proteins in the skin (OECD442C) Haptenation: covalent modification of epidermal proteins	Keratinocyte responses (OECD442D) • Activation of inflammatory cytokines •Induce cytoprotective genes	Dendritic cells (DCs) (OECD442E) • Induction of inflammatory cytokines •Mobilization of DCs	Proliferation of antigen-specific T cells (OECD429) •Histocompatibility complex representation by DCs •Activation of T cells •Proliferation of activated T cells	Inflammation upon challenge allergen To maximise the use of existing knowledge, we also incorporate historical HRIPT (human repeated insult patch test) and HMT (human maximization test)	The Bayesian model is a consensus model integrating predictions from all the other assays for an integrative qualitative risk assessment (QRA) of skin sensitization based on the weight of evidence (WoE).
•Exposure consideration ? •Physicochemical and Biopharmaceutical properties ? •Skin Penetration ? •Skin Metabolism ? 	**Prediction DPRA** Sensitizer (+) (AD, Confiability) (Outside , 92.2%) Probability map 	**Prediction KeratinoSens** Non-Sensitizer (-) (AD, Confiability) (Outside, 84.1%) Probability map 	**Prediction h-CLAT** Non-Sensitizer (-) (AD, Confiability) (Inside, 60.4%) Probability map 	**Prediction LLNA** Non-Sensitizer (-) (AD, Confiability) (Outside, 99.3%) Probability map 	**Prediction HRIPT/HMT** Sensitizer (+) (AD, Confiability) (Outside, 96.0%) Probability map 	**Bayesian Outcome** Sensitizer (+) (Confiability) (High)

Low (-) confidence prediction for the Bayesian model means two or more individual predictions are in disagreement with Bayesian Outcome.

APPENDIX I: OECD Toolbox Respiratory Sensitization Results for Propylene Carbonate (CAS #108-32-7)

Filter endpoint tree...	1 [target]
Structure	
Structure info	
Additional Ids	
CAS Number	108-32-7
CAS Smiles relation	Moderate
Chemical name(s)	1,3-Dioxolan-2-one, 4-methyl-
Composition	
Molecular Formula	C4H6O3
Predefined substance type	Mono constituent
SMILES	CC1COC(=O)O1
Parameters	
Physical Chemical Properties	
Environmental Fate and Transport	
Ecotoxicological Information	
Human Health Hazards	
Profile	
Endpoint Specific	
Respiratory sensitisation	No alert found

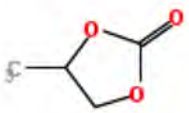
APPENDIX J: ECOSAR Modeling Results for Propylene Carbonate (CAS #108-32-7)

Organic Module Report

Results of Organic Module Evaluation

CAS	Name	SMILES
108327	1,3-Dioxolan-2-one, 4-methyl-	O=C(OCC1C)O1

Structure



Details	
Mol Wt	102.09
Selected LogKow	-0.41
Selected Water Solubility (mg/L)	200000
Selected Melting Point (°C)	-48.8
Estimated LogKow	0.08
Estimated Water Solubility (mg/L)	595691.31
Measured LogKow	-0.41
Measured Water Solubility (mg/L)	175000
Measured Melting Point (°C)	-48.8

Class Results:	

Esters

Organism	Duration	End Point	Concentration (mg/L)	Max Log Kow	Flags
Fish	96h	LC50	348.76	5	
Daphnid	48h	LC50	938.41	5	
Green Algae	96h	EC50	585.06	6.4	
Fish		ChV	43.51	8	
Daphnid		ChV	1283.22	8	
Green Algae		ChV	68.58	8	
Fish (SW)	96h	LC50	614.94	5	

1/ 2

Class Results:	

Organism	Duration	End Point	Concentration (mg/L)	Max Log Kow	Flags
Mysid	96h	LC50	1981.22	5	
Fish (SW)		ChV	57.12	8	
Mysid (SW)		ChV	19827248	8	• Chemical may not be soluble enough to measure this predicted effect. If the effect level exceeds the water solubility by 10X, typically no effects at saturation (NES) are reported
Earthworm	14d	LC50	7964.71	6	

APPENDIX K: EPI Suite™ Modeling Results for Propylene Carbonate (CAS #108-32-7)

(Estimated values included in the GreenScreen® are highlighted and bolded)

CAS Number: 108-32-7
SMILES : CC1COC(=O)O1
CHEM :
MOL FOR: C4 H6 O3
MOL WT : 102.09
---------- EPI SUMMARY (v4.11) ----------
Physical Property Inputs:
Log Kow (octanol-water): -0.41
Boiling Point (deg C) : 242.00
Melting Point (deg C) : -49.00
Vapor Pressure (mm Hg) : ------
Water Solubility (mg/L): 200
Henry LC (atm-m3/mole) : ------

Log Octanol-Water Partition Coef (SRC):
Log Kow (KOWWIN v1.69 estimate) = 0.08
Log Kow (Exper. database match) = -0.41
Exper. Ref: HANSCH,C ET AL. (1995)

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
Boiling Pt (deg C): 297.49 (Adapted Stein & Brown method)
Melting Pt (deg C): 19.56 (Mean or Weighted MP)
VP(mm Hg,25 deg C): 0.0417 (Mean VP of Antoine & Grain methods)
VP (Pa, 25 deg C) : 5.55 (Mean VP of Antoine & Grain methods)
MP (exp database): -48.8 deg C
BP (exp database): 242 deg C
VP (exp database): 4.50E-02 mm Hg (6.00E+000 Pa) at 25 deg C

Water Solubility Estimate from Log Kow (WSKOW v1.42):
Water Solubility at 25 deg C (mg/L): 5.957e+005
log Kow used: -0.41 (user entered)
melt pt used: -49.00 deg C
Water Sol (Exper. database match) = 1.75e+005 mg/L (25 deg C)
Exper. Ref: RIDDICK,JA ET AL. (1986)

Water Sol Estimate from Fragments:
Wat Sol (v1.01 est) = 1.7481e+005 mg/L

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

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
Bond Method : 3.63E-004 atm-m3/mole (3.68E+001 Pa-m3/mole)
Group Method: Incomplete

Exper Database: 3.45E-08 atm-m3/mole (3.50E-003 Pa-m3/mole)
For Henry LC Comparison Purposes:
User-Entered Henry LC: not entered
Henrys LC [via VP/WSol estimate using User-Entered or Estimated values]:
HLC: 2.801E-005 atm-m3/mole (2.838E+000 Pa-m3/mole)
VP: 0.0417 mm Hg (source: MPBPVP)
WS: 200 mg/L (source: User-Entered)

Log Octanol-Air Partition Coefficient (25 deg C) [KOAWIN v1.10]:
Log Kow used: -0.41 (user entered)
Log Kaw used: -5.851 (exp database)
Log Koa (KOAWIN v1.10 estimate): 5.441
Log Koa (experimental database): None

Probability of Rapid Biodegradation (BIOWIN v4.10):
Biowin1 (Linear Model) : 0.6989
Biowin2 (Non-Linear Model) : 0.8262
Expert Survey Biodegradation Results:
Biowin3 (Ultimate Survey Model): 2.9736 (weeks)
Biowin4 (Primary Survey Model) : 3.7004 (days-weeks)
MITI Biodegradation Probability:
Biowin5 (MITI Linear Model) : 0.4553
Biowin6 (MITI Non-Linear Model): 0.5699
Anaerobic Biodegradation Probability:
Biowin7 (Anaerobic Linear Model): 0.6759
Ready Biodegradability Prediction: NO

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

Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:
Vapor pressure (liquid/subcooled): 6 Pa (0.045 mm Hg)
Log Koa (Koawin est): 5.441
Kp (particle/gas partition coef. (m3/ug)):
Mackay model : 5E-007
Octanol/air (Koa) model: 6.78E-008
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model : 1.81E-005
Mackay model : 4E-005
Octanol/air (Koa) model: 5.42E-006

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant = 3.7871 E-12 cm3/molecule-sec
Half-Life = 2.824 Days (12-hr day; 1.5E6 OH/cm3)
Half-Life = 33.891 Hrs
Ozone Reaction:
No Ozone Reaction Estimation
Fraction sorbed to airborne particulates (phi):

2.9E-005 (Junge-Pankow, Mackay avg)
5.42E-006 (Koa method)
Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (KOCWIN v2.00):
Koc : 5.117 L/kg (MCI method)
Log Koc: 0.709 (MCI method)
Koc : 2.945 L/kg (Kow method)
Log Koc: 0.469 (Kow method)

Aqueous Base/Acid-Catalyzed Hydrolysis (25 deg C) [HYDROWIN v2.00]:
Rate constants can NOT be estimated for this structure!

Bioaccumulation Estimates (BCFBAF v3.01):
Log BCF from regression-based method = 0.500 (BCF = 3.162 L/kg wet-wt)
Log Biotransformation Half-life (HL) = -1.5709 days (HL = 0.02686 days)
Log BCF Arnot-Gobas method (upper trophic) = -0.039 (BCF = 0.9145)
Log BAF Arnot-Gobas method (upper trophic) = -0.039 (BAF = 0.9145)
log Kow used: -0.41 (user entered)

Volatilization from Water:
Henry LC: 3.45E-008 atm-m3/mole (Henry experimental database)
Half-Life from Model River: 1.715E+004 hours (714.5 days)
Half-Life from Model Lake : 1.872E+005 hours (7798 days)

Removal In Wastewater Treatment:
Total removal: 1.85 percent
Total biodegradation: 0.09 percent
Total sludge adsorption: 1.76 percent
Total to Air: 0.00 percent
(using 10000 hr Bio P,A,S)

Level III Fugacity Model: (MCI Method)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	**0.662**	**67.8**	**1000**
Water	**34.9**	**360**	**1000**
Soil	**64.3**	**720**	**1000**
Sediment	**0.0715**	**3.24e+003**	**0**

Persistence Time: 563 hr

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

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	0.662	67.8	1000
Water	34.9	360	1000

water (34.9)
biota (6.8e-007)
suspended sediment (0.000268)

Soil	64.3	720	1000
Sediment	0.0715	3.24e+003	0

Persistence Time: 563 hr

Level III Fugacity Model: (EQC Default)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	0.709	67.8	1000
Water	40	360	1000
water	(40)		
biota	(7.77e-007)		
suspended sediment	(9.56e-006)		
Soil	59.3	720	1000
Sediment	0.0733	3.24e+003	0

Persistence Time: 531 hr

Licensed GreenScreen® Profilers

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