TRIACETIN

(CAS #102-76-1)

GREENSCREEN® FOR SAFER CHEMICALS (GREENSCREEN®) ASSESSMENT

Prepared by:

ToxServices LLC

Assessment Date: December 29, 2020

Expiration Date: December 29, 2025

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GreenScreen® Executive Summary for Triacetin (CAS #102-76-1)

Triacetin is a clear, colorless liquid that is water soluble. It is not a volatile organic compound (VOC) and is not flammable. Triacetin functions as an antimicrobial, film forming agent, fragrance, plasticizer, and solvent in cosmetic products. It is used as a plasticizer for cigarette filters and cellulose nitrate. It is also used in photographic films and as a solvent in the manufacture of celluloid, a fixative in perfumery, and as a food additive.

Triacetin has low hazard concerns for all human health and environmental toxicity and fate endpoints. However, triacetin has an incomplete toxicological dataset, and ToxServices used data on its metabolites, glycerin and acetic acid, to fill the data gap for carcinogenicity. Nevertheless, data gaps remain for endocrine activity and neurotoxicity (single and repeated exposures).

Triacetin was assigned a **GreenScreen Benchmark™ Score of 3_{DG}** ("Use but Still Opportunity for Improvement" due to data gaps). It was initially assigned a preliminary Benchmark™ Score of 4 ("Prefer – Safer Chemical") before data gap analysis. This score is based on the following hazard score combinations:

- Benchmark 4
  - Low Group I Human Toxicity (carcinogenicity-C, mutagenicity-M, reproductive toxicity-R, and developmental toxicity-D)
  - Low Group II and II* Human Toxicity (acute toxicity-AT, single and repeated dose systemic toxicity-STs and STr*, skin sensitization-SnR*, respiratory sensitization-SnR*, skin irritation-IrS, and eye irritation-IrE)
  - Low Ecotoxicity (acute aquatic toxicity-AA and chronic aquatic toxicity-CA)
  - Very Low Fate Concerns (persistence-P and bioaccumulation-B)
  - Low Physical Hazards (reactivity-Rx and flammability-F)

Data gaps (DG) exist for endocrine activity-E, single dose neurotoxicity-Ns, and repeated dose neurotoxicity – Nr*. As outlined in GreenScreen® Guidance Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis), triacetin does not meet requirements for a GreenScreen Benchmark™ Score of 4 due to the hazard data gaps. However, triacetin meets the requirements for a GreenScreen Benchmark™ Score of 3. In a worst-case scenario, if triacetin were assigned a High score for the data gap E, it would be categorized as a Benchmark 1 Chemical.

GreenScreen® Hazard Summary Table for Triacetin

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
						single	repeat*	single	repeat*										
L	**L**	*L*	*L*	DG	**L**	**L**	*L*	DG	DG	**L**	*L*	**L**	**L**	**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 Triacetin (CAS #102-76-1)

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

GreenScreen® Assessment (v.1.4) Prepared By:
Name: Sara Ciotti, Ph.D.
Title: Toxicologist
Organization: ToxServices LLC
Date: November 9, 2020, December 15, 2020

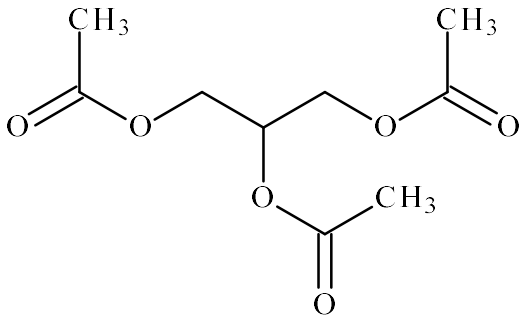
Quality Control Performed By:
Name: Bingxuan Wang, Ph.D., D.A.B.T.
Title: Senior Toxicologist
Organization: ToxServices LLC
Date: November 12, 2020, December 29, 2020

Expiration Date: December 29, 2025[2]

Chemical Name: Triacetin

CAS Number: 102-76-1

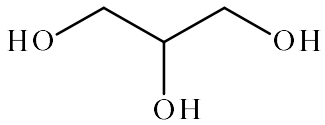
Chemical Structure(s):



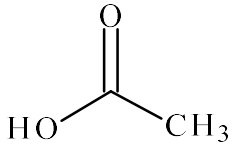
Also called: 1,2,3-Propanetriol triacetate; Acetic, 1,2,3-propanetriyl ester; Triacetin; 1,2,3-Propanetriyl triacetate; Glycerin triacetate; Glycerol triacetate; Glyceryl triacetate; Triacetyl glycerine; Triacetylglycerol (ChemIDplus 2020)

Suitable surrogates or moieties of chemicals used in this assessment (CAS #'s):
No carcinogenicity data were identified for triacetin; therefore, ToxServices identified glycerin (CAS #56-81-5) and acetic acid (CAS #64-19-7) as surrogates. Triacetin is expected to be hydrolyzed to glycerin and acetic acid following ingestion (OECD 2002a). No toxicokinetic studies on triacetin are available; however, triacetin was completely hydrolyzed to glycerin and acetic acid when it was incubated with the sacs of everted rat intestine for 1 hour at 37°C. Additionally, triacetin underwent intravascular hydrolysis in dogs (OECD 2002a). Therefore, ToxServices considers glycerin and acetic acid to be strong surrogates.

[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).



Glycerin (CAS #56-81-5)



Acetic acid (CAS #64-19-7)

Identify Applications/Functional Uses:
1. Antimicrobial (EC 2020)
2. Film forming agent (EC 2020)
3. Fragrance (EC 2020)
4. Plasticizer (EC 2020, OECD 2002a)
5. Solvent (EC 2020)
6. Food additive (OECD 2002a)

Known Impurities[3]:
No information is available. The screen is performed on the theoretical pure substance.

GreenScreen® Summary Rating for Triacetin[4,5 6,7]: Triacetin was assigned a **GreenScreen Benchmark™ Score of 3_{DG}** ("Use but Still Opportunity for Improvement" due to data gaps). It was assigned a preliminary Benchmark™ Score of 4 ("Prefer – Safer Chemical") before data gap analysis (CPA 2018b). This score is based on the following hazard score combinations:

- Benchmark 4
  - Low Group I Human Toxicity (carcinogenicity-C, mutagenicity-M, reproductive toxicity-R, and developmental toxicity-D)
  - Low Group II and II* Human Toxicity (acute toxicity-AT, single and repeated dose systemic toxicity-STs and STr*, skin sensitization-SnR*, respiratory sensitization-SnR*, skin irritation-IrS, and eye irritation-IrE)
  - Low Ecotoxicity (acute aquatic toxicity-AA and chronic aquatic toxicity-CA)
  - Very Low Fate Concerns (persistence-P and bioaccumulation-B)
  - Low Physical Hazards (reactivity-Rx and flammability-F)

Data gaps (DG) exist for endocrine activity-E, single dose neurotoxicity-Ns, and repeated dose neurotoxicity – Nr*. As outlined in GreenScreen® Guidance Section 11.6.2.1 and Annex 5 (Conduct a

[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.

Data Gap Analysis), triacetin does not meet requirements for a GreenScreen Benchmark™ Score of 4 due to the hazard data gaps. However, it meets the requirements for a GreenScreen Benchmark™ Score of 3. In a worst-case scenario, if triacetin were assigned a High score for the data gap E, it would be categorized as a Benchmark 1 Chemical.

Figure 1: GreenScreen® Hazard Summary Table for Triacetin

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
						single	repeat*	single	repeat*										
L	**L**	*L*	*L*	DG	**L**	**L**	*L*	DG	DG	**L**	*L*	**L**	**L**	**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

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

Introduction

Triacetin functions as an antimicrobial, film forming agent, fragrance, plasticizer, and solvent in cosmetic products (EC 2020). It is used as a plasticizer for cigarette filters and cellulose nitrate (OECD 2002a). It is also used in photographic films and as a solvent in the manufacture of celluloid, a fixative in perfumery, and a food additive (OECD 2002a).

ToxServices assessed triacetin 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 (SCIL)

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).

Triacetin is not listed on the SCIL.

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 2020) 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 triacetin can be found in Appendix C.

- Triacetin is an LT-UNK chemical when screened using Pharos, and therefore a full GreenScreen® is required.
- Triacetin is not listed on the U.S. DOT list.
- Triacetin is on the following lists for multiple endpoints.
    - German FEA - Substances Hazardous to Waters – Class 1 – Low Hazard to Waters
    - EC – CEPA DSL - Inherently Toxic to Humans (iTH)
- Specified lists for single endpoints are reported in individual hazard endpoints in the hazard assessment section below.

Hazard Statement and Occupational Control

No harmonized or self-assigned H statements (from its REACH registration dossier or by the majority of its notifiers in the EU) or occupational exposure limits were identified. The recommended personal protective equipment is summarized in Table 2, below.

Table 1: H Statements for Triacetin (CAS #102-76-1)

H Statement	H Statement Details
	None identified

Table 2: Occupational Exposure Limits and Recommended Personal Protective Equipment for Triacetin (CAS #102-76-1)

Personal Protective Equipment (PPE)	Reference	Occupational Exposure Limits (OEL)	Reference
Eye protection; handle with nitrile gloves; impervious clothing; respiratory protection not required	Millipore Sigma 2020	None identified	

Physicochemical Properties of Triacetin

Triacetin is a clear colorless liquid that is water soluble. Its relatively low vapor pressure indicates that it has low volatility, but may exist as a gas under ambient conditions. Based on its partition coefficient (log K_{ow} = 0.21) it is more soluble in octanol than in water.

Table 3: Physical and Chemical Properties of Triacetin (CAS #102-76-1)

Property	Value	Reference
Molecular formula	$C_9H_{14}O_6$	ChemIDplus 2020
SMILES Notation	CC(=O)OCC(COC(=O)C)OC(=O)C	ChemIDplus 2020
Molecular weight	218.20 g/mol	ChemIDplus 2020
Physical state	Liquid	ECHA 2020a
Appearance	Clear, colorless	ECHA 2020a
Melting point	-78ºC	ECHA 2020a
Boiling point	258 - 259ºC	ECHA 2020a

[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 Triacetin (CAS #102-76-1)		
Property	**Value**	**Reference**
Vapor pressure	0.0025 mmHg[9]	ECHA 2020a
Water solubility	58,000 mg/L @ 25ºC	ECHA 2020a
Dissociation constant	No dissociation	ECHA 2020a
Density/specific gravity	1.161 g/cm³ at 20°C	ECHA 2020a
Partition coefficient	Log K_{ow} = 0.21	OECD 2002a

Toxicokinetics

No toxicokinetic studies on triacetin are available; however, triacetin was completely hydrolyzed to glycerin and acetic acid when it was incubated with the sacs of everted rat intestine for 1 hour at 37°C. Additionally, triacetin underwent intravascular hydrolysis in dogs (OECD 2002a).

Hazard Classification Summary

Group I Human Health Effects (Group I Human)

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

Triacetin was assigned a score of Low for carcinogenicity based on negative results in rat and mouse studies using the surrogate glycerin. Additionally, the long history of use of acetic acid as a food additive and negative results in repeated dose toxicity studies in rats and rabbits indicate that it is non-carcinogenic. 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 because it is based on experimental data on glycerin and a long history of safe use for acetic acid.

- 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 2020b, OECD 2002b
  - *Oral: Surrogate: Glycerin (CAS #56-81-5):* Glycerin was evaluated in a 2 year carcinogenicity study (1 year for high dose group) in which male and female Long-Evans rats (22/sex/dose; 26/sex/controls) were administered 5, 10, and 20% glycerin (natural: purity not reported; synthetic: 99.5% purity) in the diet (equivalent to 2,000, 4,000, and 8,000 mg/kg for males and 2,500, 5,000, and 10,000 mg/kg for females as calculated by study authors). Animals were observed daily, weighed weekly, and examined pathologically (liver, spleen, adrenals, kidney, small intestine, gonads, urinary bladder) upon death or at study conclusion. No increase in tumor formation was observed in rats administered natural or synthetic glycerin compared to controls (Klimisch 2, reliable with restrictions)
- OECD 2002b
  - *Oral: Surrogate: Glycerin (CAS #56-81-5):* Glycerin was evaluated as part of a study of tumor promoting effects of glycerol in which a group of male ddY mice (number not reported) was administered 5% glycerin in water for 20 weeks. Treatment with glycerol alone did not increase the number of tumor bearing mice compared to controls. Additional details were not provided.
- ECB 2000
  - *Oral: Surrogate: Acetic acid (CAS #64-19-7):* Acetic acid was evaluated in a chronic

[9] 0.3306 Pa / 133 = 0.0025 mm Hg

rabbits study. Rabbits (strain/sex/number not reported) received acetic acid (purity not reported) at 100 – 700 mg/kg/day in drinking water for 13 months and no tumors were found. No further details were provided for the study.
    - *Oral: Surrogate: Acetic acid (CAS #64-19-7):* Acetic acid was evaluated in a 5-month gavage study in rabbits (strain/sex/number not reported). Animals received 100 – 200 mg/kg acetic acid (purity not reported) twice daily. No tumors were found. No further details were provided.
    - *Oral: Surrogate: Acetic acid (CAS #64-19-7):* Acetic acid was evaluated in a 5-month gavage study in rabbits (strain/sex/number not reported). Animals received 100 – 200 mg/kg acetic acid (purity not reported) twice daily. No tumors were found. No further details were provided.
    - *Oral: Surrogate: Acetic acid (CAS #64-19-7):* Acetic acid was evaluated in a 135-day study in rats (sex/strain/number not reported). Animals received 350 mg/kg acetic acid (purity not reported) orally (unspecified) 3 times per week for 63 days and then 140 mg/kg for 72 days. No histological evidence of tumors was found. No further details were provided.
- JECFA 1974
    - *Oral: Surrogate: Acetic acid (CAS #64-19-7):* About 1 g/day of acetic acid has been consumed by humans in vinegar and other items of food and drinks without known adverse effects at these consumption levels. However, continued ingestion of large doses has been regarded as a contributory factor in the development of Laennec type of liver cirrhosis.

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

Triacetin was assigned a score of Low for mutagenicity/genotoxicity based on negative genotoxicity assays. GreenScreen® criteria classify chemicals as a Low hazard for mutagenicity/genotoxicity when negative data are available for both gene mutations and chromosome aberrations, and they are not GHS classified (CPA 2018b). The confidence in the score is high as it is based on reliable experimental data.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2020a
    - *In vitro:* Triacetin (purity not reported) in DMSO was negative in a GLP-compliant bacterial reverse mutation assay conducted in a manner similar to OECD Guideline 471 (lack of test substance details and *Salmonella typhimurium* strain TA102 and Escherichia coli were not tested) using S. typhimurium strains TA98, TA100, TA1535, and TA1537 treated with 50, 150, 1,500, and 5,000 µg/plate in the presence and absence of metabolic activation. Negative and positive controls were valid. Positive controls in the absence of metabolic activation included sodium azide (2 µg/plate) for TA1535 and TA100, 9-aminoacridine (20 µg/plate) for TA1537, and 2-nitrofluorene (5 µg/plate) for TA98. 2-Aminoanthracene (2 µg/plate) was used as the positive control for all strains in the presence of metabolic activation. No cytotoxicity or precipitate was reported. The study authors concluded that triacetin was not mutagenic under the conditions of this study (Klimisch 2, reliable with restrictions, ECHA study number 002).
    - *In vitro:* Triacetin (98.2% purity) in water was negative in a GLP-compliant bacterial reverse mutation assay conducted according to OECD Guideline 471 in *S. typhimurium* strains TA98, TA100, TA1535, and TA1537 and E. coli WP2 uvrA treated with 313, 625, 1,250, 2,500, and 5,000 µg/plate in the presence and absence of metabolic activation. The negative and positive controls were valid. In the absence of metabolic activation the following positive controls were used: 2-(2-furyl)-3-(5-nitro-2-furyl)acrylamide (0.01

μg/plate) for TA98, TA100, and WP2 uvrA, sodium azide (0.5 μg/plate) for TA1535, and 9-aminoacridine (80 μg/plate). In the presence of metabolic activation, 2-aminoacridine (0.5, 1, 2, or 10 μg/plate) was used as a positive control for all strains. The study authors concluded that triacetin was not mutagenic under the conditions of this study (Klimisch 2, reliable with restrictions, ECHA study number 007).

- ECHA 2020a, OECD 2020a
  - *In vitro:* In a GLP-compliant *in vitro* chromosome aberration assay conducted according to OECD Guideline 473, Chinese hamster lung (CHL/IU) cells were treated with triacetin (98.2% purity) in DMSO at 0.55, 1.1, and 2.2 mg/mL with and without metabolic activation. Cells were treated continuously (24 or 48 hours) without metabolic activation or short-term (6 hours) with and without metabolic activation. Negative control was valid. Positive controls were valid for the continuous exposure treatments. The wrong positive control was used during the short-term exposure without metabolic activation. Cyclophosphamide (5 μg/mL) was used as the positive control in the presence of metabolic activation and mitomycin C (0. 5 μg/mL) was used as the positive control in the absence of metabolic activation. There was no evidence of chromosome aberrations or cytotoxicity in the absence of metabolic activation. However, an increase in chromosomal aberrations was reported at the highest concentration of 2.2 mg/mL, in the presence of metabolic activation. The authors noted that cytotoxicity (75%) and low pH (4.9) were measured at the highest concentration; therefore, the chromosomal aberrations were not considered to be biologically relevant (Klimisch 2, reliable with restrictions, ECHA study number 003).
- U.S. EPA 2012
  - *In vitro:* Triacetin (purity not reported) was negative in a suspension test conducted in *Saccharomyces cerevisiae* strain D4 treated with 0, 1.25, 2.5, and 5% with and without metabolic activation. The negative and positive controls were valid. Treatment did not result in gene conversions.
  - *In vivo:* Triacetin (purity not reported) was negative in an *in vivo* mutagenicity assay conducted in 1962 using adult *Drosophila melanogaster* treated with 0.2-0.3 mg. No additional details were provided.
- Based on the weight of evidence, a score of Low was assigned. Triacetin was negative in bacterial reverse mutation assays at concentrations up to 5,000 μg/plate in the presence and absence of metabolic activation. Because an increase of chromosomal aberrations in an in vitro study was reported only at the highest concentration (2.2 mg/mL) in the presence of metabolic activation and due to the high cytotoxicity (75%) and low pH (4.9), ToxServices did not consider it to be biologically relevant. Triacetin was also negative in a suspension test in *S. cerevisiae* and in a mutation assay using *D. melanogaster*. Therefore, ToxServices assigned a score of Low as there is no evidence of genotoxicity.

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

Triacetin was assigned a score of Low for reproductive toxicity based on the absence of adverse reproductive effects in a GLP-compliant OECD Guideline 422 assay in rats. GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is low as it is based on a screening assay.

- 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 2012
    - *Oral:* In a GLP-compliant combined repeated dose and reproductive toxicity screening study conducted according to OECD Guideline 422, Crj:CD(SD) IGS Sprague Dawley rats (12/sex) were administered triacetin (> 98.2% purity) at doses of 0, 40, 200, or 1,000 mg/kg/day in 3% gum arabic in purified water via oral gavage. Treatment began 2 weeks prior to mating. Males were treated for 44 days and females were treated for 41-48 days. Treatment had no effect on copulation, fertility, implantation, number of corpora lutea, gestation length, or delivery. The U.S. EPA identified a reproduction NOAEL of 1,000 mg/kg/day, which was the highest dose tested.

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M, or L): *L*
Triacetin was assigned a score of Low for developmental toxicity based on the absence of adverse effects in a GLP-compliant OECD Guideline 422 study in rats. 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 low because it is based on a screening assay.

- 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 2020a, OECD 2002a, U.S. EPA 2012
    - *Oral:* In a GLP-compliant combined repeated dose and reproductive toxicity screening study conducted according to OECD Guideline 422, Crj:CD(SD) IGS Sprague Dawley rats (12/sex) were administered triacetin (> 98.2% purity) at doses of 0, 40, 200, or 1,000 mg/kg/day in 3% gum arabic in purified water via oral gavage. Treatment began 2 weeks prior to mating. Males were treated for 44 days and females were treated for 41-48 days. Treatment had no effect on copulation, fertility, implantation, number of corpora lutea, gestation length, or delivery. There were no effects on pup viability, offspring born alive, sex ratio, body weights, and offspring alive on postnatal day (PND) 4. Additionally, there were no treatment-related effects on pup body weights. The U.S. EPA identified a developmental NOAEL of 1,000 mg/kg/day, which was the highest dose tested (Klimisch score 1, reliable without restriction).

Endocrine Activity (E) Score (H, M, or L): DG
Triacetin was assigned a score of Data Gap for endocrine activity based on insufficient data 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 2020
    - Triacetin was active in 2/21 estrogen receptor (ER) assays, 0/15 androgen receptor (AR) assays, 0/2 steroidogenesis assays, and 0/12 thyroid receptor assays performed as part of the U.S. EPA's Endocrine Disruptor Screening Program (EDSP) in the 21st Century.
- According to CPA Guidance (CPA 2018), a score of Low requires negative data for at least the following five pathways: androgenicity, anti-androgenicity, thyroid effects, estrogenicity, and anti-estrogenicity. A score of Moderate is assigned if there is an indication of endocrine activity. As insufficient data for a Low score are available, and only very limited evidence of endocrine activity are available from *in vitro* receptor assays, ToxServices determined that insufficient data are available to assign a Low or Moderate score.

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

Triacetin was assigned a score of Low for acute toxicity based on oral and dermal LD_{50} values greater than 2,000 mg/kg. While one study reported oral LD_{50} values between 1,000 and 2,000 mg/kg in mice, and New Zealand classified triacetin to GHS Category 4 as a result, the remaining oral studies reported LD_{50} values greater than 2,000 mg/kg in both rats and mice. The overall weight of evidence suggests that triacetin is not classifiable under GHS. GreenScreen® criteria classify chemicals as a Low hazard for acute toxicity when oral and dermal LD_{50} values are greater than 2,000 (CPA 2018b). The confidence in the score is high as it is based on reliable experimental data.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* GHS – New Zealand – 6.1D (oral) – Acutely toxic.
- CCID 2020
  - GHS New Zealand classified triacetin as a 6.1D acute oral toxicant (equivalent to GHS Category 4 (NZG EPA 2019)) based on an oral LD_{50} of 1,100 mg/kg in mice.
- ECHA 2020a, OECD 2002a
  - *Oral:* LD_{50} > 2,000 mg/kg in male and female Wistar rats (GLP, OECD Guideline 401)
  - *Oral:* LD_{50} = 9,288 mg/kg in male and female mice (strain not reported)
- OECD 2002a
  - *Oral:* LD_{50} = 6,400 - 12,800 mg/kg in rats (sex and strain not reported)
  - *Oral:* LD_{50} = 3,000 mg/kg in rats
  - *Oral:* LD_{50} = 12,700 mg/kg in rats
  - *Oral:* LD_{50} = 1,800 mg/kg in male mice and 1,100 mg/kg in female mice
  - *Oral:* LD_{50} = 3,200 – 6,400 mg/kg in mice
- CIR 2003, OECD 2002a
  - *Dermal:* LD_{50} > 5,000 mg/kg in rabbits
  - *Dermal:* LD_{50} = 20 mL/kg (equivalent to 23,220 mg/kg)[10] in guinea pigs
- ECHA 2020a
  - *Inhalation:* LC_{50} (aerosol) > 1.7 mg/L in male and female Wistar rats (GLP, OECD 403)

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

Triacetin was assigned a score of Low for systemic toxicity (single dose) based on the absence of adverse systemic effects in an acute oral toxicity study in rats. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (single dose) when no adverse systemic effects occur at oral doses up to 2,000 mg/kg (CPA 2018b). The confidence in the score is high as it is based on a well-conducted oral toxicity 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 2020a, OECD 2002a
  - *Oral:* In a GLP-compliant acute oral toxicity study according to OECD Guideline 401, male

[10] 20 mL/kg * 1.161 g/cm3 * 1 cm3/1 mL * 1,000 mg/g = 23,220 mg/kg

and female Wistar rats (5/sex) were administered a single dose of triacetin (100% purity) at 2,000 mg/kg via oral gavage. Animals were observed for 14 days. All animals survived the treatment period and no adverse clinical signs were reported. Treatment had no effect on body weight gain and no treatment-related effects were identified at necropsy. The study authors identified an LD_{50} of > 2,000 mg/kg. No additional details were provided (Klimisch score 1, reliable without restriction).

- OECD 2002a
  - *Oral:* In an acute oral toxicity study in rats (5/dose, strain and sex not reported), treatment with 800 – 12,800 mg/kg triacetin (purity not reported) caused fatality, weakness, and ataxia. An oral LD_{50} of 6,400-12,800 mg/kg was identified. No additional details were provided.
- ECHA 2020a
  - *Inhalation:* In a GLP-compliant acute inhalation toxicity study conducted in 1985 in a manner similar to OECD Guideline 403 (lack of details on the test substance), male and female Wistar Bor: WISW (SPF-Cpb) rats (5/sex/group) were exposed to triacetin (purity not reported) aerosol at 1.7 mg/L (analytical) via nose only inhalation for 4 hours. Animals were monitored for 14 days. All animals were alive at the end of the study period. There were no clinical signs of toxicity and no effects on body weight. Treatment caused no local irritation of the visible mucous membranes of the respiratory tract. The study authors identified an LC_{50} of > 1.7 mg/L (Klimisch 2, reliable with restrictions).
- Based on the weight of evidence, a score of Low was assigned. No evidence of systemic toxicity was identified at up to 2,000 mg/kg in rats in a GLP-compliant acute oral toxicity study conducted according to OECD Guideline 401. Insufficient data are available to determine if triacetin is classifiable for single exposure systemic toxicity via inhalation exposure. An acute inhalation toxicity study conducted according to OECD Guideline 403 reported no adverse systemic effects in rats exposed to 1.7 mg/L triacetin aerosol for 4 hours. As 1.7 mg/L is greater than the GHS guidance value of 1.0 mg/L (dust/mist/fume) for Category 1 classification, but the study did not test up to the guidance value of 5.0 mg/L for Category 2 classification, data are insufficient to determine if triacetin is classifiable under GHS.

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

Triacetin was assigned a score of Low for systemic toxicity (repeated dose) based on the absence of adverse systemic effects in oral and inhalation repeated dose toxicity studies. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (repeated dose) when no adverse systemic effect occur at oral doses > 100 mg/kg/day and inhalation concentrations > 1 mg/L/6h/day in 90-day studies (CPA 2018b). The confidence in the score is low because the inhalation studies provided limited details and do not comply with current guidelines.

- 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 2012
  - *Oral:* In a peer-reviewed study, triacetin (purity not reported) was administered to a 13-month-old girl for 6 months and an 8-month-old boy for 4.5 months in infant formula. The subjects were initially administered 25 mg/kg twice daily (50 mg/kg/day) for the first week, and the dose was doubled each subsequent week up to a maximum dose of 250 mg/kg twice daily (500 mg/kg/day). Both subjects in this study had been previously diagnosed with Canavan disease, a fatal dysmyelinating genetic disorder. The disease is characterized by mutations in the enzyme aspartoacylase, which results in the reduced or absent ability to

hydrolyze N-acetylaspartate to acetate and aspartate. Triacetin is a known acetate precursor. The goal of the study was to determine if low-dose triacetin is well-tolerated in infants having Canavan disease. This study received approval by an Institutional Review Board and parental consent. Triacetin was well-tolerated and no adverse effects were identified. The United States Environmental Protection Agency (U.S. EPA) identified a NOAEL of 500 mg/kg/day.

- *Oral:* In a second clinical tolerability study of triacetin in infants with Canavan disease, triacetin (purity not reported) was administered to a 12-month old boy for 6 months and an 8-month old girl for 4.5 months. The initial dose was 500 mg/kg four times daily (2,000 mg/kg/day) for the first 3 days, followed by a doubling of the dose every 3 days up to a maximum dose of 4,500 mg/kg/day. The original maximum dose was 5,000 mg/kg/day; however, the children experienced "discomfort" at that dose. No adverse effects were reported at a daily dose of 4,500 mg/kg/day. The highest tested dose of 5,000 mg/kg/day caused discomfort potentially related to gastric acidity. The authors identified a NOAEL of 4,500 mg/kg/day. No LOAEL was identified.
- *Oral:* In a repeated dose toxicity study, male Sprague-Dawley rats (n=8, number per group not reported) received a control diet, a diet with 30% of the energy as corn oil, or a diet with 30% as short chain triglycerides (95% triacetin and 5% corn oil) for 30 days. The triacetin diet contained 19% triacetin, which was reported to be equivalent to 16,367 mg/kg/day. There were no treatment-related effects on mortality, clinical signs, body weights, food consumption, lactate, ketone bodies, glucose concentrations, mean villus height, intestinal crypt depth, and carcass composition. In the triacetin treatment group, plasma free fatty acids were decreased (44%) and plasma triglycerides were increased (22%). Additionally, the DNA content was increased (68%) in the colon mucosa, RNA content was decreased (33%) in the jejunum, and protein: DNA ratio was decreased (38%) in the jejunum. The U.S. EPA identified a NOAEL of 16,367 mg/kg/day, which was the only dose tested. However, the U.S. EPA noted that this study provided limited information for the assessment of triacetin toxicity.
- *Oral:* In a repeated dose toxicity study using the same methodology as the 30-day study described above, male Sprague-Dawley rats (n=8, number per group not reported) were administered a control diet, a diet with 30% of the energy as corn oil, or a diet with 30% as short chain triglycerides (95% triacetin and 5% corn oil) for 30 days. The triacetin diet contained 19% triacetin, which was reported to be equivalent to 16,367 mg/kg/day. The study authors evaluated the adipose cell size and number for epididymal, perirenal, and inguinal fat depots. No treatment-related effects were reported. The U.S. EPA identified a NOAEL of 16,367 mg/kg/day, which was the only dose tested. However, the U.S. EPA noted that this study provided limited information for the assessment of triacetin toxicity.
- *Oral:* In a GLP-compliant combined repeated dose and reproductive toxicity screening study conducted according to OECD Guideline 422, Crj:CD(SD) IGS Sprague Dawley rats (12/sex) were administered triacetin (> 98.2% purity) at doses of 0, 40, 200, or 1,000 mg/kg/day in 3% gum arabic in purified water via oral gavage. Treatment began 2 weeks prior to mating. Males were treated for 44 days and females were treated for 41-48 days. One high dose male rat was found dead on day 32; however, no evidence of systemic toxicity was identified in any other animals and its death was considered incidental to treatment. No adverse clinical signs were reported and treatment had no effect on body weights, body weight gain, food consumption, or organ weights. No gross or histopathological findings were identified. Significant decreases in the percent of band neutrophils and creatine were measured in the 40 and 1,000 mg/kg/day males. Additionally, significant increases in inorganic phosphorus were measured in the 200 mg/kg/day males.

However, these changes were within physiological ranges and were not dose-dependent. The study authors identified a systemic NOAEL of 1,000 mg/kg/day, which was the highest dose tested. *The U.S. EPA (2012) selected this study as the principal study for the derivation of screening level subchronic and chronic provisional reference doses (p-RfD).*

- *Oral:* In a subchronic toxicity study, male Sprague-Dawley rats (8/group) were exposed to triacetin (purity not reported) in the diet for 13 weeks. This study investigated the feasibility of replacing starch with alternate carbohydrate sources and six different diets were tested: Diet 1 (control, 60% starch), Diet 2 (30% glycerol and 30% propylene glycol), Diet 3 (30% glycerol and 30% triacetin), Diet 4 (30% propylene glycol and 30% triacetin), Diet 5 (40% glycerol and 20% propylene glycol), and Diet 6 (40% glycerol and 20% triacetin). Equivalent doses of triacetin in diets containing it at 20% and 30% were 17,228 and 25,843 mg/kg/day, respectively. The diets all contained 27% casein and 5% safflower oil with identical amounts of cellulose, salts, and vitamins. Decreased (20%) body weights were measured in animals fed Diets 3 and 6 (glycerol and triacetin) during weeks 12 and 13. No body weight changes were measured in animals fed Diet 4 (propylene glycol and triacetin). Additionally, changes in body weight gains were reported in triacetin groups; however, the U.S. EPA (2012) noted that due to other variables in the diets (i.e., casein, glycerol, and propylene glycol) it is difficult to determine if the changes are due to triacetin alone. The study authors and U.S. EPA (2012) identified no NOAEL or LOAEL and the U.S. EPA noted that insufficient toxicological parameters were evaluated. Due to the previously mentioned study deficiencies, ToxServices did not identify a NOAEL or LOAEL for this study.
- *Oral:* In a repeated dose toxicity study, wild-type and tremor rat pups (6-12 males or females/group) were orally administered triacetin twice daily at 4.2 g/kg on PND 7-14, then 5.8 g/kg on PND 15-23, and then animals were exposed via their food (7.5%) and water (5%) for a total treatment period of 110-120 days. The equivalent doses in food and water were 7,099 mg/kg/day and 7,504 mg/kg/day, respectively, totally an oral dose of 14,603 mg/kg/day after PND 23. The tremor rat model mimics Canavan disease in humans (described previously). Therefore, this study was designed to support the efficacy of oral triacetin supplementation for aspartate deficiency. There were no treatment-related effects on mean blood chemistry values and no microscopic lesions were identified in any of the examined tissues (brain, spinal cord, lung, heart, liver, kidney, stomach, small and large intestine, and spleen). Slight decreases in food consumption and body weights were measured in triacetin treatment groups; however, the effects were not statistically significant. The study authors reported that triacetin treatment had no adverse effects under the conditions of this study. The U.S. EPA (2012) identified a NOAEL of 14,603 mg/kg/day based on the absence of adverse effects. However, the U.S. EPA (2012) noted that the study provided limited information and was missing GLP status, test compound purity, and rat husbandry conditions. Additionally, hematology, urinalysis, organ weights, and necropsy were not performed or their results were not reported. Furthermore, the histology analysis was not adequate as it was limited to 10 tissues and only tissues from 2-4 rats were examined.
- *Inhalation:* In a subchronic inhalation toxicity study, rats (strain, sex, and number not reported) were exposed to triacetin (purity not reported) vapor via whole-body inhalation at 249 ppm for 6 hours per day, 5 days per week, for 90 days. OECD (2002a) reported 249 ppm to be equivalent to 2,220 mg/m^3 and ToxServices calculated 249 ppm to be equivalent to 2.22 mg/L ((ppm)(MW) / 24,450 = (249 ppm)(218.204) / 24,450 = 2.22 mg/L). Inhalation exposure was extended one week at 73.72 ppm and 8,271 ppm (equivalent to 0.66 and 74 mg/L, respectively) ((73.72 ppm)(218.204) / 24,450 = 0.66 mg/L and (8,271

ppm)(218.204)/24,450 = 73.81 mg/L). No concurrent control group was used. No adverse clinical signs were reported. Treatment had no effect on hematology (red and white blood cell counts and hemoglobin) or urine (albumin and sugar) parameters or liver and kidney weights. Additionally, no histopathological findings were identified in the trachea, bronchi, lung, kidney, liver, and bladder. The study authors identified a NOAEC of 249 ppm (2.22 mg/L) (OECD 2002a, U.S. EPA 2012). Adjusting for a daily exposure, the NOAEC of 2.22 mg/L is equivalent to 1.59 mg/L/day (2.22 mg/L * 5 days / 7 days = 1.59 mg/L/day).

- *Inhalation:* In a repeated dose toxicity study, three rats (strain and sex not reported) were exposed to 250 ppm triacetin (purity not reported) via inhalation for 6 hours per day, 5 days per week, for 64 days. ToxServices calculated 250 ppm to be equivalent to 2.23 mg/L ((250 ppm)(218.204) / 24,450 = 2.23 mg/L). An additional three rats were exposed to 8,271 ppm triacetin (equivalent to 74 mg/L) for 6 hours per day for 64 days ((73.72 ppm) (218.204) / 24,450 = 0.66 mg/L; (8,271 ppm) (218.204) / 24,450 = 73.81 mg/L). No adverse effects were reported. No additional details were provided. The study authors identified a NOAEC of 8,271 ppm (74 mg/L) (U.S. EPA 2012). Adjusting for a daily exposure, the NOAEC of 74 mg/L is equivalent to 53 mg/L/day (74 mg/L * 5 days / 7 days = 53 mg/L/day).
- *Inhalation:* In a repeated dose toxicity study, rats (strain, sex, number not reported) were exposed to triacetin (purity not reported) via inhalation at 250 ppm, for 6 hours per day, 5 days per week, for 13 weeks. ToxServices calculated 250 ppm to be equivalent to 2.23 mg/L((250 ppm)(218.204)/24,450 = 2.23 mg/L). No adverse clinical signs were reported. Treatment had no effect on liver or kidney weights. No histopathological changes were reported and there were no treatment-related effects on blood counts or urine analysis. No additional details were provided. The study authors identified a NOAEC of 250 ppm (2.23 mg/L) (U.S. EPA 2012). Adjusting for a daily exposure, the NOAEC of 2.23 mg/L is equivalent to 1.59 mg/L/day (2.23 mg/L * 5 days / 7 days = 1.59 mg/L/day).

- Based on the weight of evidence, a score of Low was assigned. Clinical studies indicate that triacetin is well-tolerated in infants (≥ 6 months old) at oral doses up to 4,500 mg/kg for 4.5 months. A GLP-compliant repeated dose toxicity study with a reproductive and developmental toxicity screening assay conducted according to OECD Guideline 422 identified no adverse systemic effects in animals treated orally with up to 1,000 mg/kg/day triacetin. As GHS guidance values are based on 90 days studies, they were multiplied by 2.2 (90 days / 41 days = 2.2) in order to account for study duration (i.e., 10 – 100 mg/kg/day adjusted to 22 – 220 mg/kg/day). Based on the oral NOAEL of 1,000 mg/kg/day, no classification is warranted because the NOAEL is greater than 220 mg/kg/day. Additionally, no evidence of systemic toxicity was reported in inhalation repeated dose toxicity studies with triacetin at up to 53 mg/L/day in a 64-day study and 1.59 mg/L/day in 90-day studies. As 1.59 mg/L/day is greater than the GHS guidance value of 1 mg/L/day (vapor), no classification is warranted. Based on the weight of evidence, a score of Low was assigned. Confidence in this classification is low because the inhalation studies provided limited details and do not comply with current guidelines. Additional oral repeated dose toxicity studies were identified; however, limited study details were provided and the U.S. EPA (2012) noted many study deficiencies.

Neurotoxicity (single dose, N-single) (Group II) Score (vH, H, M, or L): DG
Triacetin was assigned a score of Data Gap for neurotoxicity (single dose) based on insufficient data 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.

- OECD 2002a
    - *Oral:* In an acute oral toxicity study in rats (5/dose, strain and sex not reported), treatment with 800 – 12,800 mg/kg triacetin (purity not reported) caused fatality, weakness, and ataxia. An oral LD_{50} of 6,400-12,800 mg/kg was identified. No additional details were provided.
- Based on the weight of evidence, a score of Data Gap was assigned. Ataxia and weakness were reported in an acute oral toxicity study in rats; however, no information on the reversibility of the effects was provided. GHS criteria state that if narcotic effects (Category 3) are not transient in nature, they should be considered for classification as Category 1 or 2 (UN 2019). As it is unknown if the effect are transient and if the effects were reported in animals that survived the study (i.e., they did not occur immediately before death), insufficient information is available for classification.

Neurotoxicity (repeated dose, N-repeated) (Group II*) Score (H, M, or L): DG
Triacetin was assigned a score of Data Gap for neurotoxicity (repeated dose) based on a lack of data 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.
- No data were identified for triacetin or its surrogates, glycerin and acetic acid.

Skin Sensitization (SnS) (Group II*) Score (H, M, or L): L
Triacetin was assigned a score of Low for skin sensitization based on a negative maximization test in humans and multiple negative tests in guinea pigs. GreenScreen® criteria classify chemicals as a Low hazard for skin sensitization 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 consistent experimental data.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.
- OECD 2002a
    - A case report identified one case of allergic eczema in a 29-year old woman. The woman was allergic to triacetin used in the production of cigarette filters.
- CIR 2003
    - Triacetin (purity not reported) was not sensitizing in five guinea pigs using the "drop-on method". No additional details were provided.
    - Triacetin (purity not reported) in acetone, dioxane, and guinea pig fat (7:2:1) was not sensitizing in guinea pigs. Animals were dosed three times over a 5 day period and then challenged after 1, 2, or 3 weeks. A vehicle and positive control was used. No additional details were provided.
    - Authors of the Cosmetic Ingredient Review (CIR) state that there are additional reports that triacetin is not sensitizing in guinea pigs; however, no details were provided.
    - Undiluted triacetin (purity not reported) was not sensitizing in a maximization test conducted in 33 subjects. Triacetin was applied to the forearm of subjects for 48 hours under occlusive conditions on 5 alternate days. As triacetin is not irritating to the skin, 2% sodium lauryl sulfate was applied to the test and challenge sites for 24 hours or 30 min, respectively, prior to treatment. After a 10-14 day non-treatment period, individuals were challenged at a previously unexposed site on the back. SDS and petroleum patches were used as controls. Undiluted triacetin was not irritating or sensitizing under the conditions of this study.

- Undiluted triacetin was not sensitizing in a maximization test in humans or in multiple tests in guinea pigs. Therefore, it is not classified as a skin sensitizer.

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

Triacetin was assigned a score of Low for respiratory sensitization based on the lack of dermal sensitization potential according to the ECHA guidance (2017). GreenScreen® criteria classify chemicals as a Low hazard for respiratory sensitization when they are not GHS classified (CPA 2018b). The confidence in the score is low as this evaluation does not include non-immunologic mechanisms of respiratory sensitization, and no specific data are available for respiratory sensitization.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- OECD 2020
  - Triacetin does not contain any structural alerts for respiratory sensitization (Appendix D).
- 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 triacetin was not sensitizing to the skin (see skin sensitization section above), and a literature search did not find any human evidence of respiratory sensitization by triacetin, and as triacetin does not contain any structural alerts for respiratory sensitization (OECD 2020), triacetin is not expected to be a respiratory sensitizer.

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

Triacetin was assigned a score of Low for skin irritation/corrosivity based on the results of skin irritation studies in humans and animals. GreenScreen® criteria classify chemicals as a Low hazard for skin irritation/corrosivity when adequate data are available and negative and they are not GHS classified (CPA 2018b). The confidence in the score is high because it is based on reliable experimental data.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2020a, OECD 2002a
  - In a GLP-compliant acute skin irritation assay conducted in a manner similar to OECD Guideline 404 (missing details on the test substance, no tabulation of individual scores, and occlusive dressing used), undiluted triacetin (purity not reported) was applied to the shaved skin of Kleinrusse, Chbb:HM rabbits (n=4, sex not reported) for 4 hours under occlusive conditions. Animals were monitored for 3 days. Mild erythema was reported in 1 of 4 animals 1 hour after treatment. No other signs of irritation were identified and mean (24, 48, and 72 hour) erythema and edema scores of 0 were reported. (Klimisch 2, reliable with restrictions).
- OECD 2002a, CIR 2003
  - In an acute skin irritation study, triacetin (purity not reported) caused skin irritation (erythema, slight edema, alopecia, and desquamation) in guinea pigs. Groups comprising 2-3 animals were used. However, no study details were provided. The study was completed in 1967.

- CIR 2003
    - In an acute dermal irritation study, doses of 5 and 10 cc/kg triacetin (purity and vehicle not reported) was applied to the skin of guinea pigs (n=2, sex and strain not reported) under occlusive conditions for 24 hours. Treatment caused slight edema and erythema was reported at the high dose. No additional details were provided.
    - In a Dehring-chamber test, triacetin (purity not reported) was applied as a 50% dilution (vehicle not reported) to the skin of 20 human volunteers. Treatment caused very mild skin reactions. No additional details were provided.
- OECD 2002a
    - Triacetin (purity not reported) was not irritating in a human patch test. No study details were provided.
- Based on the weight of evidence, a score of Low was assigned. In a well-conducted GLP-compliant guinea pig skin irritation test, triacetin caused mild skin irritation that was fully reversible within 24 hours. The mean (24, 48, and 72 hour) erythema and edema scores were 0. Two additional guinea pig studies reported that triacetin caused mild skin irritation; however, very limited study details were provided. In one human patch test, triacetin caused no skin irritation and in a Dehring-chamber test it caused very mild skin reactions in humans. Very limited details were provided for the clinical studies. GHS criteria (UN 2019) state that chemicals should be classified as a mild skin irritant (Category 3) when they cause a "mean score of ≥ 1.5 and < 2.3 for erythema/eschar or edema in at least 2 of 3 tested animals from gradings at 24, 48, and 72 hours or, if reactions are delayed, from grades on 3 consecutive days after the onset of skin reactions". As the GLP-compliant skin irritation study in guinea pigs reported mean erythema and edema scores of 0 and additional studies with very limited details reported no irritation to mild irritation, ToxServices did not classify triacetin.

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

Triacetin was assigned a score of Low for eye irritation/corrosivity based on negative animal studies. GreenScreen® criteria classify chemicals as a Low hazard for eye irritation/corrosivity 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 well-conducted 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 2020a, OECD 2002a
    - In a GLP-compliant acute eye irritation study conducted in 1988 in a manner similar to OECD Guideline 405 (lacking test substance details), undiluted triacetin (0.1 mL, purity not reported) was instilled into the eyes of Kleinrusse, Chbb:HM rabbits (n=4, sex not reported) and animals were monitored to 3 days. Treatment caused slight irritation that was fully reversible within 24 hours. Mean cornea opacity, iris, conjunctivae, and redness scores of 0 were reported. The study authors concluded that triacetin was not irritating to the eyes under the conditions of this study (Klimisch 2, reliable with restrictions).
- CIR 2003
    - In an acute eye irritation study, undiluted triacetin (purity not reported) was instilled into the conjunctival sac of rabbits (n=6, sex and strain not reported) and the irritation was scored using the Draize methodology. Corneal thickness was also measured. The study authors reported a Draize score of 1 after 2 hours (0 for cornea and 0.7 for the conjunctiva). The corneal thickness did not change. No additional details were reported.
- OECD 2002a, CIR 2003

  - Additional eye irritation tests found that triacetin caused no irritation to mild irritation in rabbits. However, minimal to no study details were provided. Additionally, a commercial product that contains triacetin, diacetin, and monoacetin caused severe burning, pain, and redness of the conjunctiva. No injury was reported. The study authors reported that diacetin causes considerably more discomfort than triacetin.
- Based on the weight of evidence, a score of Low was assigned. Triacetin was not irritating to the eyes of rabbits in a well-conducted study conducted in a manner similar to OECD Guideline 405. Additional animal studies reported that triacetin caused no irritation to mild irritation; however, limited study details were provided. One case report stated that a commercial product containing triacetin caused eye discomfort and redness of the conjunctiva; however, the authors claimed that the product also contains diacetin which causes more discomfort than triacetin. As triacetin was not irritating to the eyes of rabbits in a GLP-compliant study conducted in a manner similar to OECD Guideline 405, ToxServices did not classify triacetin.

Ecotoxicity (Ecotox)

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

Triacetin was assigned a score of Low for acute aquatic toxicity based on acute aquatic toxicity values > 100 mg/L in fish, aquatic invertebrates, and algae. GreenScreen® criteria classify chemicals as a Low hazard for acute aquatic toxicity when acute aquatic toxicity values are > 100 mg/L (CPA 2018b). The confidence in the score is high as based on experimental data.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2020a, NITE 2010, OECD 2002a
  - Triacetin (98% purity) was evaluated for acute aquatic toxicity in fish in a GLP-compliant study conducted according to OECD Guideline 203. The 96-hour LC_{50} in *Oryzias latipes* (Orange killifish/Japanese medaka) was >100 mg/L (nominal) (Klimisch 1, reliable without restriction).
  - Triacetin (purity not reported) was evaluated for acute aquatic toxicity to daphnia in a GLP-compliant study performed according to OECD Guideline 202. The 48-hour EC_{50} in *Daphnia magna* was 770 mg/L. No additional details were provided (Klimisch 4, not assignable).
- ECHA 2020a, OECD 2002a
  - Triacetin (± 100% ester (purity)) was evaluated for acute aquatic toxicity in fish in a GLP-compliant study conducted in a manner similar to an "old national guideline". The 48-hour LC_{50} in *Cyprinus carpio* (carp) was 174 mg/L (nominal) (Klimisch 2, reliable with restrictions).
  - Triacetin (99.5% purity) was evaluated for acute aquatic toxicity to daphnia in a GLP-compliant study performed according to EPA Method C.2. The 48-hour EC_{50} in *D. magna* was 380 mg/L (nominal) (Klimisch 2, reliable with restrictions).
- OECD 2002a
  - Triacetin (>99.5% purity) was evaluated for acute aquatic toxicity in fish in a GLP-compliant study conducted according to OECD Guideline 203. The 96-hour LC_{50} in *Pimephales promelas* (Fathead minnow) was 165.3 mg/L.
  - Triacetin (purity not reported) was evaluated for acute aquatic toxicity in fish conducted according to OECD Guideline 203. The 96-hour LC_{50} in *Brachydanio rerio* (Zebrafish) was 300 mg/L.

  - Triacetin (purity not reported) was evaluated for acute aquatic toxicity in fish conducted according to DIN38412 Teil15. The 48-hour LC_{50} in *Leuciscus idus* (Golden orfe) was 170 mg/L.
  - Triacetin (> 99.5% purity) was evaluated for acute aquatic toxicity to daphnia in a GLP-compliant study performed according to OECD Guideline 202. The 48-hour EC_{50} in *D. magna* was 810.9 mg/L.
- ECHA 2020a
  - Triacetin (98% purity) was evaluated in a GLP-compliant acute toxicity test in algae conducted according to OECD Guideline 201. The 72-hour growth rate and biomass EC_{50} values in *Pseudokirchneriella subcapitata* were > 940 mg/L (measured) (Klimisch 1, reliable without restriction).

Chronic Aquatic Toxicity (CA) Score (vH, H, M, or L): L
Triacetin was assigned a score of Low for chronic aquatic toxicity based on chronic aquatic toxicity study values > 10 mg/L in fish, aquatic invertebrates, and algae. GreenScreen® criteria classify chemicals as a Low hazard for chronic aquatic toxicity when chronic aquatic toxicity study values are > 10 mg/L in fish, aquatic invertebrates, and algae (CPA 2018b). The confidence in the score is high because it is based on measured data in fish, daphnia and algae.

- 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 2020a, NITE 2010, OECD 2002a
  - Triacetin (> 98% purity) was evaluated in a GLP-compliant prolonged fish toxicity test conducted according to OECD Guideline 204. The 14-day NOEC was 100 mg/L (nominal) (Klimisch 1, reliable without restriction).
  - Triacetin (98% purity) was evaluated in a GLP-compliant *D. magna* reproduction test conducted according to OECD Guideline 211. The 21-day NOEC was ≥ 94 mg/L (measured) (Klimisch 1, reliable without restriction).
- ECHA 2020a
  - Triacetin (98% purity) was evaluated in a GLP-compliant acute toxicity test in algae conducted according to OECD Guideline 201. The 72-hour growth rate and biomass NOEC values in *Pseudokirchneriella subcapitata* were 468 mg/L (measured) (Klimisch 1, reliable without restriction).
- NITE 2010
  - Triacetin (purity not reported) was evaluated in a GLP-compliant acute toxicity test in algae conducted according to OECD Guideline 201. The 72-hour growth rate and biomass NOEC values in algae (species not reported) were 460 mg/L and 560 mg/L, respectively. No additional details were provided.
- U.S. EPA 2017a
  - Triacetin belongs to the esters ECOSAR chemical class. The most conservative predicted chronic values (ChVs) are 28 mg/L in fish, 715 mg/L in daphnia, and 54.3 mg/L in green algae (Appendix E).

<u>Environmental Fate (Fate)</u>

Persistence (P) Score (vH, H, M, L, or vL): vL
Triacetin was assigned a score of Very Low for persistence based on the results of ready biodegradation tests. GreenScreen® criteria classify chemicals as a Very Low hazard for persistence when they

primarily partition to soil and meet the 10-day window in ready biodegradation tests (CPA 2018b). The confidence in the score is high because it is based on high quality 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 2020a
  - Triacetin (purity not reported) was readily biodegradable and met the 10-day window in a ready biodegradability CO_2 evolution test conducted in a manner similar to OECD Guideline 301B (only one control flask). The reference substance performed appropriately. Triacetin was 62-64% degraded on day 9 and 76-82% degraded on day 29 (Klimisch 2, reliable with restrictions).
  - Triacetin (>99% purity) was readily biodegradable but did not meet the 10-day window in a GLP-compliant ready biodegradability CO_2 evolution test conducted in a manner similar to OECD Guideline 301B (only one blank control flask). Triacetin was tested at 10 mg/L and 20 mg/L. On days 2, 5, 12, 16, and 28 the 10 mg/L sample was 2.5%, 24.3%, 48.7%, 63.1%, and 63.1-63.7% degraded, respectively. On days 2, 5, 12, 16, and 28 the 20 mg/L sample was 0.5%, 15.8%, 64.4%, 77.4%, and 86.8-93.3% degraded, respectively. The 20 mg/L sample but not the 10 mg/L sample met the 10-day window. Therefore, the study authors concluded that triacetin was readily biodegradable but did not meet the 10-day window under the conditions of this study (Klimisch 2, reliable with restrictions).
- OECD 2002a
  - Triacetin (> 98% purity) was readily biodegradable in a modified MITI test conducted according to OECD Guideline 301C with 77% degradation after 14 days based on BOD and 94% degradation after 14 days based on TOC.
  - Triacetin (purity not reported) was readily biodegradable in a ready biodegradation study conducted according to OECD Guideline 301D with 4-5% degradation after 5 days, 57-62% degradation after 15 days, and 69-79% degradation after 30 days.
- U.S. EPA 2017b
  - The BIOWIN modeling Ready Biodegradable Predictor indicates that triacetin is expected to be readily biodegradable. Fugacity modeling (MCI method) predicts 76.1% will partition to soil with a half-life of 30 days, 23.6% will partition to water with a half-life of 15 days, and 0.214% will partition to air with a half-life of 30.2 days (Appendix F).
- Based on the weight of evidence, a score of Very Low was assigned. Fugacity modeling predicts triacetin will partition primarily to soil. Triacetin was readily biodegradable and met the 10-day window in a GLP compliant ready biodegradation test. When the major compartment is soil, GreenScreen® criteria specify a score of Very Low if the chemical meets the 10-day window in a ready biodegradation test.

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

Triacetin was assigned a score of Very Low for bioaccumulation based on the measured partition coefficient of 0.21 and predicted BCFs values of 3.162 and 0.9241. GreenScreen® criteria classify chemicals as a Very Low hazard for bioaccumulation when the partition coefficient is less than 4 and the BCF is less than 100 (CPA 2018b). The confidence in the score is high because it is based on a measured partition coefficient.

- 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 2002a

    - Log K_{ow} = 0.21 (OECD Guideline 107)
- U.S. EPA 2017b
    - The BCF estimated using the EPI Suite™ regression-based method is 3.162 L/kg wet-wt and using the Arnot-Gobas method (upper trophic), taking into consideration of metabolism, is 0.9241, based on the measured log K_{ow} of 0.21 (Appendix F).

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M, or L): *L*
Triacetin was assigned a score of Low for reactivity based on the absence of reactive functional groups in the molecular structure. GreenScreen® criteria classify chemicals as a Low hazard for reactivity when they are non-explosive and non-reactive (CPA 2018b). The confidence in the score was low as no measured data were identified.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.
- ECHA 2020a
    - Triacetin contains no chemical groups associated with oxidizing or explosive properties.
- No measured data were identified. Therefore, screening procedures for explosivity were used here to estimate the reactivity property of triacetin. These procedures are listed in the GHS (UN 2019).
    - Based on the structure of its components or moieties, triacetin is not considered explosive or self-reactive due to lack of functional groups associated with explosive or self-reactive properties (See Appendix G).
    - Based on the structure of its components or moieties, triacetin is not considered to have oxidizing properties as it does not contain any structural groups known to be correlated with a tendency to react exothermally with combustible materials.

Flammability (F) Score (vH, H, M, or L): L
Triacetin was assigned a score of Low for flammability based on its flash point. GreenScreen® criteria classify chemicals as a Low hazard for flammability when it is non-flammable (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 2020a
    - The flash point of triacetin (purity not reported) was 148°C when measured in a closed cup test per ASTM D 3828 (Klimisch 2, reliable with restrictions).
    - The flash point of triacetin (purity not reported) was 137.78-148.89°C when measured in an open cup test (guideline not reported) (Klimisch 2, reliable with restrictions).
- Based on the weight of evidence, a score of Low was assigned. Triacetin is not flammable based on a flash point > 93°C (UN 2019).

Use of New Approach Methodologies (NAMs)[11] in the Assessment

Table 4: Summary of NAMs Used in the GreenScreen® Assessment		
Endpoint	**NAMs Data Available and Evaluated? (Y/N)**	**Types of NAMs Data (*in silico* modeling/*in vitro* biological profiling/frameworks)**
Carcinogenicity	N	Not applicable
Mutagenicity	N	Not applicable
Reproductive toxicity	N	Not applicable
Developmental toxicity	N	Not applicable
Endocrine activity	N	Not applicable
Acute mammalian toxicity	N	Not applicable
Single exposure systemic toxicity	N	Not applicable
Repeated exposure systemic toxicity	N	Not applicable
Single exposure neurotoxicity	N	Not applicable
Repeated exposure neurotoxicity	N	Not applicable
Skin sensitization	N	Not applicable
Respiratory sensitization	Y	*In silico* modeling: OECD Toolbox structural alerts
Skin irritation	N	Not applicable
Eye irritation	N	Not applicable
Acute aquatic toxicity	N	Not applicable
Chronic aquatic toxicity	Y	*In silico* modeling: ECOSAR
Persistence	Y	*In silico* modeling: EPI Suite™ Non-animal testing: OECD 301B and 301C Biodegradation tests
Bioaccumulation	Y	*In silico* modeling: EPI Suite™

[11] 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).

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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 Triacetin (CAS #102-76-1)

TOXSERVICES
TOXICOLOGY RISK ASSESSMENT CONSULTING

GreenScreen® Score Inspector

Table 1: Hazard Table

			Group I Human					Group II and II* Human								Ecotox		Fate		Physical	
			Carcinogenicity	Mutagenicity/Genotoxicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
Table 2: Chemical Details									S	R *	S	R *	*	*								
Inorganic Chemical?	Chemical Name	CAS#	C	M	R	D	E	AT	STs	STr	Ns	Nr	SNS*	SNR*	IrS	IrE	AA	CA	P	B	Rx	F
No	Triacetin	102-76-1	L	L	*L*	*L*	DG	L	L	*L*	DG	DG	L	*L*	L	L	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	No	No			
4	STOP						

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
Triacetin	4

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

Table 6

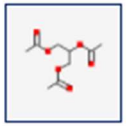
Chemical Name	Final GreenScreen® Benchmark Score
Triacetin	3DG

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												
4	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	3DG

APPENDIX C: Pharos Output for Triacetin (CAS #102-76-1)



102-76-1
Triacetin
ALSO CALLED [2102168-03-4] Triacetin (primary CASRN is 102-76-1), 1,2,3-Propanetriol triacetate, 1,2,3-Propanetr...
View all synonyms (25)

Share Profile

Hazards | Properties | Functional Uses | Process Chemistry | Resources

Pharos Hazards View

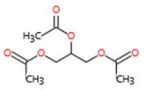
Download Lists

ENDPOINT	HAZARD LEVEL	HAZARD LIST	HAZARD DESCRIPTION	OTHER LISTS
Mammalian	Medium	GHS - New Zealand	6.1D (oral) - Acutely toxic	
Terrestrial	Medium	GHS - New Zealand	9.3C - Harmful to terrestrial vertebrates	
Positive list	Low	Cosmetic Ingredient Review (CIR)	Safe as Used	+2
	Low	Inventory of Existing Cosmetic Ingredients in China (IECIC 2015)	Cosmetic Ingredients	
	Very Low	US EPA - DfE SCIL	Green Circle - Verified Low Concern	
Multiple	Potential Concern	EC - CEPA DSL	Inherently Toxic to Humans (iTH)	+1
	Potential Concern	German FEA - Substances Hazardous to Waters	Class 1 - Low Hazard to Waters	

Positive Lists (3)

- Cosmetic Ingredient Review (CIR): Safe as Used
- Inventory of Existing Cosmetic Ingredients in China (IECIC 2015): Cosmetic Ingredients
- US EPA - DfE SCIL: Green Circle - Verified Low Concern

APPENDIX D: OECD Toolbox Respiratory Sensitization Results for Triacetin (CAS #102-76-1)

Filter endpoint tree...	1 [target]
Structure	
Respiratory sensitisation	No alert found

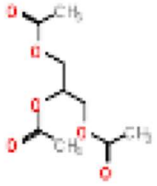
APPENDIX E: ECOSAR Modeling Results for Triacetin (CAS #102-76-1)

Organic Module Result | Experimental Data | Physical Properties | Kow Estimate | Report

Esters

Organism	Duration	End Point	Concentratio...	Max Log Kow	Flags
Fish	96h	LC50	264	5.0	
Daphnid	48h	LC50	653	5.0	
Green Algae	96h	EC50	360	6.4	
Fish		ChV	28.0	8.0	
Daphnid		ChV	715	8.0	
Green Algae		ChV	54.3	8.0	
Fish (SW)	96h	LC50	443	5.0	
Mysid	96h	LC50	977	5.0	
Fish (SW)		ChV	47.3	8.0	
Mysid (SW)		**ChV**	**2.02E+6**	**8.0**	⚠
Earthworm	14d	LC50	9.59E+3	6.0	

CAS	Name	SMILES
102761	1,2,3-Propanetriol, triacetate	O=C(OCC(OC(=O)C)COC(=O)C)C

Structure


Details	
Mol Wt	218.21
Selected LogKow	0.36
Selected Water Solubility (mg/L)	58000
Selected Melting Point (°C)	78
Estimated LogKow	0.36
Estimated Water Solubility (mg/L)	41600.37
Measured LogKow	0.25
Measured Water Solubility (mg/L)	58000
Measured Melting Point (°C)	78

Class Results:	

Esters

Organism	Duration	End Point	Concentration (mg/L)	Max LogKow	Flags
Fish	96h	LC50	263.62	5	
Daphnid	48h	LC50	652.98	5	
Green Algae	96h	EC50	360.18	6.4	
Fish		ChV	27.96	8	
Daphnid		ChV	714.93	8	
Green Algae		ChV	54.26	8	
Fish (SW)	96h	LC50	443.33	5	

Class Results:	

Organism	Duration	End Point	Concentration (mg/L)	Max LogKow	Flags
Mysid	96h	LC50	976.88	5	
Fish (SW)		ChV	47.33	8	
Mysid (SW)		ChV	2020924.62	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	9590.47	6	

APPENDIX F: EPI Suite™ Modeling Results for Triacetin (CAS #102-76-1)

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

CAS Number: 102-76-1
SMILES : CC(=O)OCC(COC(=O)C)OC(=O)C
CHEM :
MOL FOR: C9 H14 O6
MOL WT : 218.21
---------- EPI SUMMARY (v4.11) ----------

Physical Property Inputs:
Log Kow (octanol-water): 0.21
Boiling Point (deg C) : 258.00
Melting Point (deg C) : -78.00
Vapor Pressure (mm Hg) : 0.0025
Water Solubility (mg/L): 58000
Henry LC (atm-m3/mole) : ------

Log Octanol-Water Partition Coef (SRC):
Log Kow (KOWWIN v1.69 estimate) = 0.36
Log Kow (Exper. database match) = 0.25
Exper. Ref: HANSCH,C ET AL. (1995)

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
Boiling Pt (deg C): 238.15 (Adapted Stein & Brown method)
Melting Pt (deg C): -37.29 (Mean or Weighted MP)
VP(mm Hg,25 deg C): 0.0177 (Mean VP of Antoine & Grain methods)
VP (Pa, 25 deg C) : 2.36 (Mean VP of Antoine & Grain methods)
MP (exp database): -78 deg C
BP (exp database): 259 deg C
VP (exp database): 2.48E-03 mm Hg (3.31E-001 Pa) at 25 deg C

Water Solubility Estimate from Log Kow (WSKOW v1.42):
Water Solubility at 25 deg C (mg/L): 1.397e+005
log Kow used: 0.21 (user entered)
melt pt used: -78.00 deg C
Water Sol (Exper. database match) = 5.8e+004 mg/L (25 deg C)
Exper. Ref: RIDDICK,JA ET AL. (1986)

Water Sol Estimate from Fragments:
Wat Sol (v1.01 est) = 56100 mg/L

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

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
Bond Method : 1.75E-009 atm-m3/mole (1.77E-004 Pa-m3/mole)
Group Method: 5.11E-011 atm-m3/mole (5.18E-006 Pa-m3/mole)

Exper Database: 1.23E-08 atm-m3/mole (1.25E-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: 1.238E-008 atm-m3/mole (1.254E-003 Pa-m3/mole)
VP: 0.0025 mm Hg (source: User-Entered)
WS: 5.8E+004 mg/L (source: User-Entered)

Log Octanol-Air Partition Coefficient (25 deg C) [KOAWIN v1.10]:
Log Kow used: 0.21 (user entered)
Log Kaw used: -6.299 (exp database)
Log Koa (KOAWIN v1.10 estimate): 6.509
Log Koa (experimental database): None

Probability of Rapid Biodegradation (BIOWIN v4.10):
Biowin1 (Linear Model) : 1.1662
Biowin2 (Non-Linear Model) : 1.0000
Expert Survey Biodegradation Results:
Biowin3 (Ultimate Survey Model): 3.1376 (weeks)
Biowin4 (Primary Survey Model) : 4.2198 (days)
MITI Biodegradation Probability:
Biowin5 (MITI Linear Model) : 1.0119
Biowin6 (MITI Non-Linear Model): 0.9711
Anaerobic Biodegradation Probability:
Biowin7 (Anaerobic Linear Model): 0.9991
Ready Biodegradability Prediction: YES

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

Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:
Vapor pressure (liquid/subcooled): 0.333 Pa (0.0025 mm Hg)
Log Koa (Koawin est): 6.509
Kp (particle/gas partition coef. (m3/ug)):
Mackay model : 9E-006
Octanol/air (Koa) model: 7.93E-007
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model : 0.000325
Mackay model : 0.000719
Octanol/air (Koa) model: 6.34E-005

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant = 8.4987 E-12 cm3/molecule-sec
Half-Life = 1.259 Days (12-hr day; 1.5E6 OH/cm3)
Half-Life = 15.102 Hrs
Ozone Reaction:
No Ozone Reaction Estimation
Fraction sorbed to airborne particulates (phi):

0.000522 (Junge-Pankow, Mackay avg)
6.34E-005 (Koa method)
Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (KOCWIN v2.00):
Koc : 40.73 L/kg (MCI method)
Log Koc: 1.610 (MCI method)
Koc : 8.13 L/kg (Kow method)
Log Koc: 0.910 (Kow method)

Aqueous Base/Acid-Catalyzed Hydrolysis (25 deg C) [HYDROWIN v2.00]:
Total Kb for pH > 8 at 25 deg C : 6.172E-001 L/mol-sec
Kb Half-Life at pH 8: 12.997 days
Kb Half-Life at pH 7: 129.965 days
(Total Kb applies only to esters, carbmates, alkyl halides)

Bioaccumulation Estimates (BCFBAF v3.01):
Log BCF from regression-based method = 0.500 (BCF = 3.162 L/kg wet-wt)
Log Biotransformation Half-life (HL) = -3.7212 days (HL = 0.00019 days)
Log BCF Arnot-Gobas method (upper trophic) = -0.034 (BCF = 0.9241)
Log BAF Arnot-Gobas method (upper trophic) = -0.034 (BAF = 0.9241)
log Kow used: 0.21 (user entered)

Volatilization from Water:
Henry LC: 1.23E-008 atm-m3/mole (Henry experimental database)
Half-Life from Model River: 7.032E+004 hours (2930 days)
Half-Life from Model Lake : 7.672E+005 hours (3.197E+004 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	**0.214**	**30.2**	**1000**
Water	**23.6**	**360**	**1000**
Soil	**76.1**	**720**	**1000**
Sediment	**0.083**	**3.24e+003**	**0**

Persistence Time: 670 hr

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

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	0.214	30.2	1000
Water	23.6	360	1000

water (23.6)
biota (1.91e-006)
suspended sediment (0.00144)
Soil 76.1 720 1000
Sediment 0.083 3.24e+003 0
Persistence Time: 670 hr

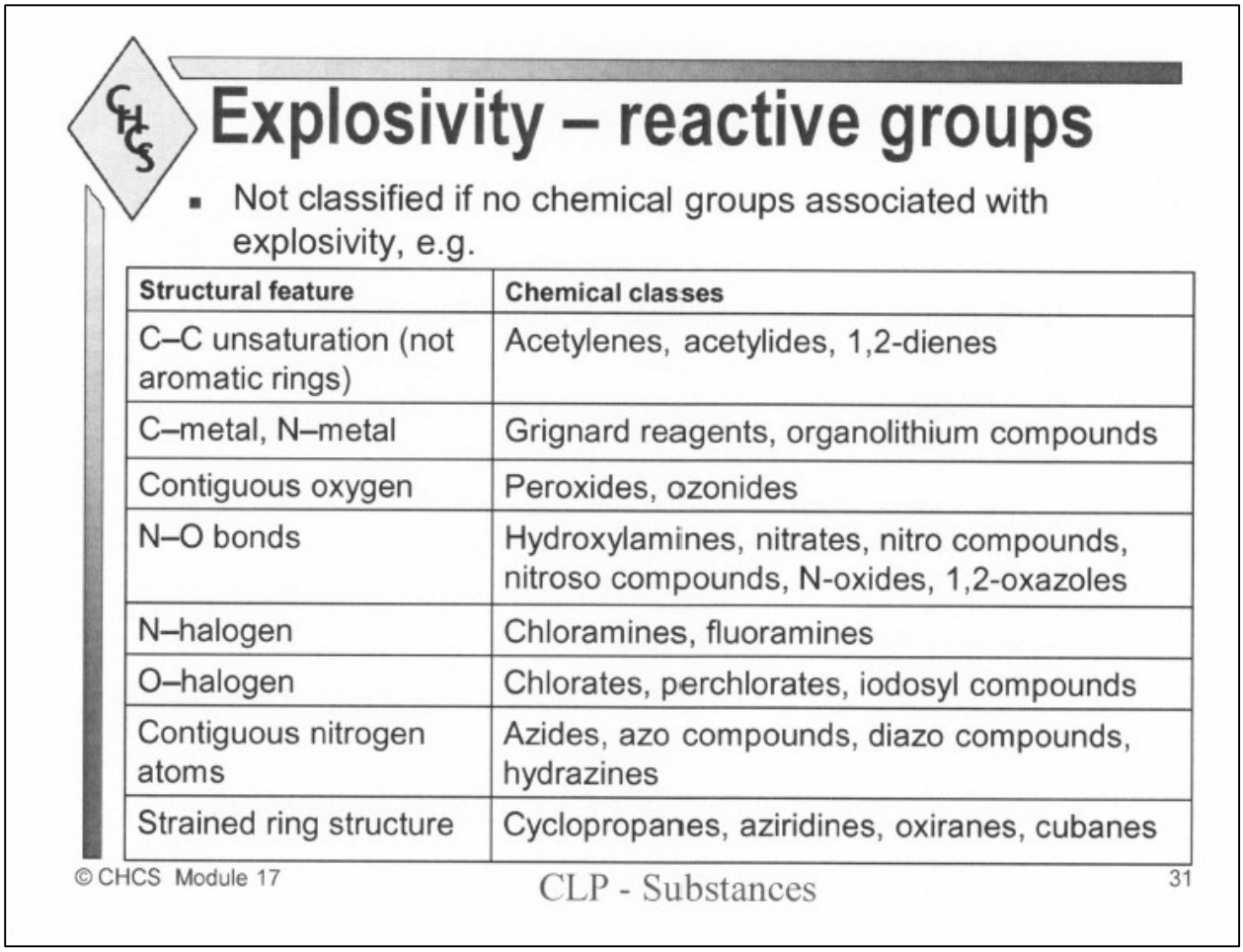
Level III Fugacity Model: (EQC Default)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	0.264	30.2	1000
Water	38.9	360	1000
water	(38.9)		
biota	(3.15e-006)		
suspended sediment	(3.88e-005)		
Soil	60.8	720	1000
Sediment	0.0722	3.24e+003	0

Persistence Time: 553 hr

APPENDIX G: Known Structural Alerts for Reactivity

Explosivity – Abbreviated List



Explosivity – reactive groups

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

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

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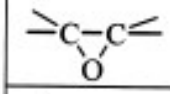
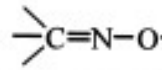
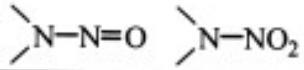
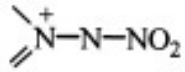
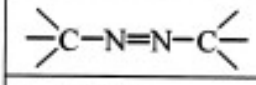
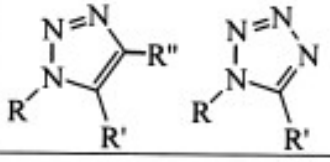
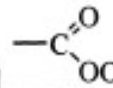
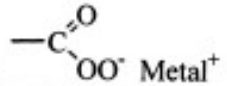
Explosivity – Full List

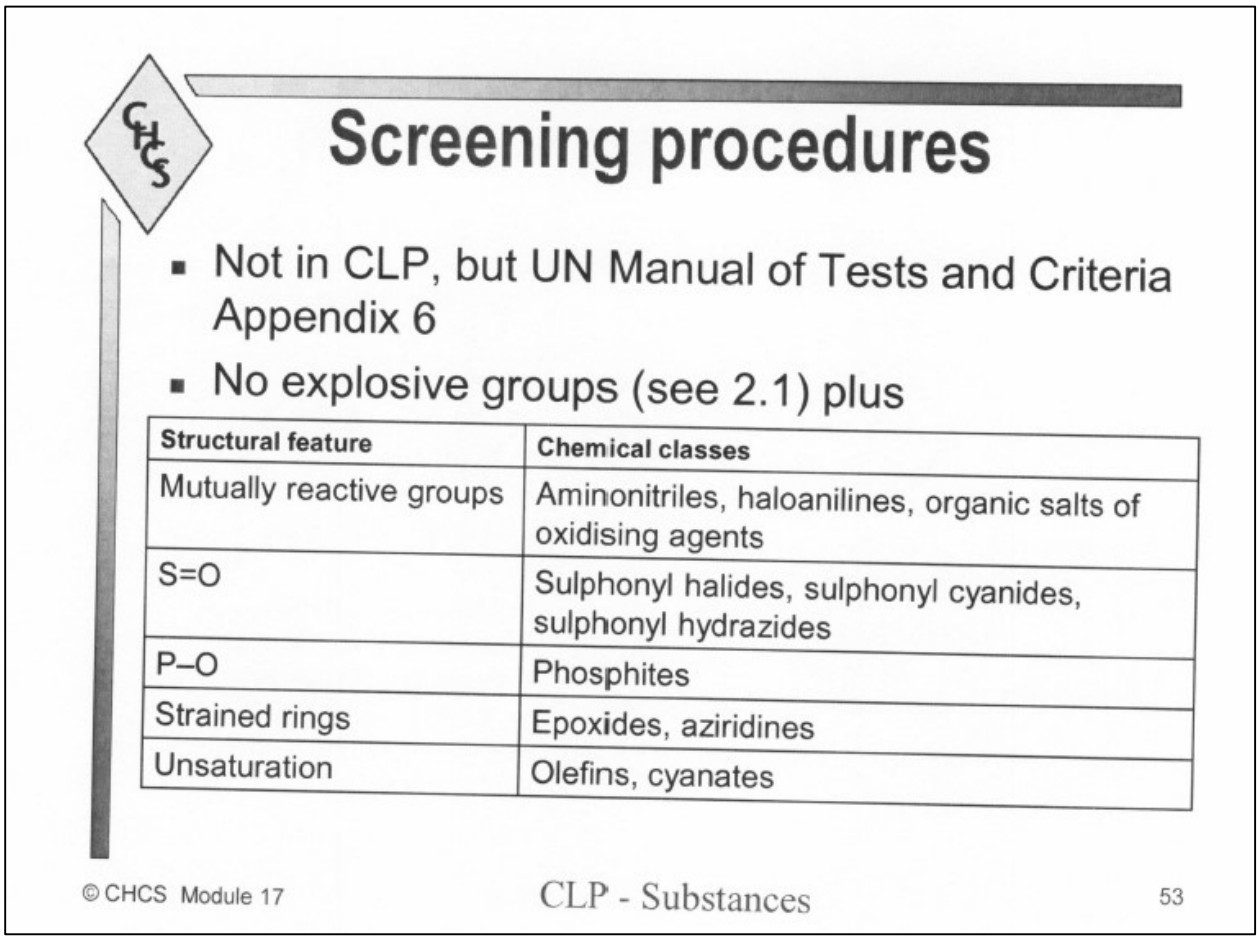
Table R.7.1-28 Chemical groups associated with explosive properties

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

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

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

Self-Reactive Substances



Licensed GreenScreen® Profilers

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