POLYCITRONELLOL ACETATE

(CAS #2417284-25-2)

GREENSCREEN® FOR SAFER CHEMICALS (GREENSCREEN®) ASSESSMENT

Prepared by:

ToxServices LLC

Assessment Date: July 9, 2025

Expiration Date: July 9, 2030

TOXSERVICES
TOXICOLOGY RISK ASSESSMENT CONSULTING
1526 New Hampshire Ave., N.W., Suite 350
Washington, D.C. 20036

TABLE OF CONTENTS

TABLE OF FIGURES

TABLE OF TABLES

GreenScreen® Executive Summary for Polycitronellol Acetate (CAS #2417284-25-2)

Polycitronellol acetate is a low molecular weight polymer that is derived from terpenoids, specifically citronellol. It is a colorless to light yellow liquid at room temperature. It is not soluble in water and decomposes at temperatures greater than 160°C. Polycitronellol acetate is used as a silicone alternative in cosmetics and personal care products as an emollient, humectant, fragrance, and hair and skin conditioning agent. Due to the low molecular weight and variable composition as a mixture, ToxServices evaluated it as a UVCB substance (unknown or variable composition, complex reaction products or biological materials).

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

- Benchmark 2c
    - High Persistence-P + High Ecotoxicity (acute aquatic toxicity-AA)
    - High P + Moderate Ecotoxicity (chronic aquatic toxicity-CA)

Data gaps (DG) exist for endocrine activity-E and neurotoxicity (repeated dose)-N (r*). As outlined in GreenScreen® Guidance Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis), polycitronellol acetate meets requirements for a GreenScreen Benchmark™ Score of 2 despite the hazard data gaps. In a worst-case scenario, if polycitronellol acetate 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 vitro* tests for genotoxicity, endocrine activity, skin sensitization, skin irritation, and eye irritation, and *in silico* modeling for respiratory sensitization, chronic aquatic toxicity, persistence, and bioaccumulation. 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 polycitronellol acetate's NAMs dataset include absence of, or inadequate experimental data for endocrine activity, skin sensitization, respiratory sensitization, skin and eye irritation, chronic aquatic toxicity, and bioaccumulation, and lack of established test methods for respiratory sensitization. Polycitronellol acetate's Type II (extrapolation output) uncertainties include limitations of *in vitro* genotoxicity assays to mimic *in vivo* metabolic conditions and their focusing on a few genotoxicity events, incomplete coverage of EDSP Tox 21 assays of critical endocrine pathways ant their uncertain *in vivo* relevance, the inability of *in vitro* skin sensitization assays in evaluating pro-haptens and pre-haptens, lack of defined applicability domains of the OECD Toolbox structural alerts for respiratory sensitization, and its lack of consideration of non-immunological mechanisms of respiratory sensitization, limitations of *in vitro* skin and eye irritation assays in determining single GHS classifications, and the inaccurate prediction of aquatic toxicities for this type of substances. Some of polycitronellol acetate'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 Polycitronellol Acetate

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**	*L*	DG	**L**	*L*	*L*	**L**	*H*	*M*	*H*	*L*	*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 Polycitronellol acetate (CAS #2417284-25-2)

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

GreenScreen® Assessment (v.1.4) Prepared By:
Name: Mitchell Kelly, M.S.
Title: Toxicologist
Organization: ToxServices LLC
Date: March 24, 2025; June 27, 2025

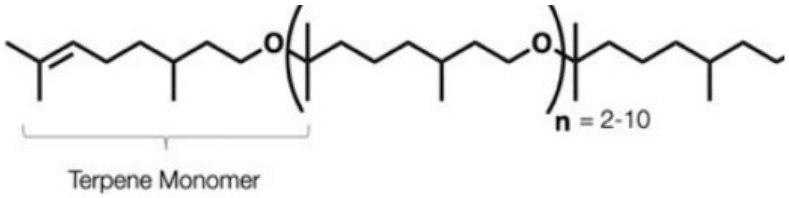
Quality Control Performed By:
Name: Bingxuan Wang, Ph.D., D.A.B.T.
Title: Senior Toxicologist
Organization: ToxServices LLC
Date: March 25, 2025; July 9, 2025

Expiration Date: July 9, 2030[2]

Chemical Name: Polycitronellol Acetate

CAS Number: 2417284-25-2

Chemical Structure(s):

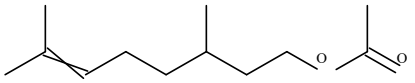


(P2 Science 2022)

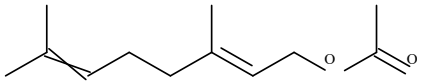
Also called:
Citronellol Polymer Acetate (P2 Science 2020); Citropol® 1A; Citropol® HA (P2 Science 2022)

Suitable surrogates or moieties of chemicals used in this assessment (CAS #'s):
Limited data are reported for polycitronellol acetate. Therefore, data on its building block citronellyl acetate (CAS #150-84-5) were used. Additionally, structurally similar monoterpenoid geranyl acetate (CAS #105-87-3) was selected to fill data gaps as it was used for read-across in the ECHA CHEM dossier for citronellyl acetate (ECCHA CHEM, CAS #150-84-5, 2025). Finally, geranyl acetate metabolites geraniol (CAS #106-24-1) and nerol (CAS #106-25-2) were also used for read-across in the ECHA CHEM dossier for citronellyl acetate and were selected as suitable surrogates when data for citronellyl acetate and geranyl acetate were not available. ToxServices considered all these surrogates conservative as they are much smaller than polycitronellol acetate, with higher water solubility, and likely higher bioavailability and reactivity.

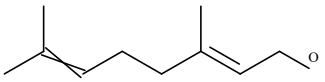
[1] GreenScreen® reports are either "UNACCREDITED" (by unaccredited person), "AUTHORIZED" (by Authorized GreenScreen® Practitioner), or "CERTIFIED" (by Licensed GreenScreen® Profiler or equivalent).
[2] Assessments expire five years from the date of completion starting from January 1, 2019. An assessment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



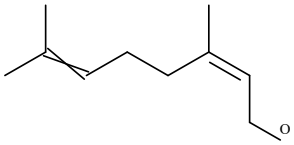
Citronellyl Acetate (CAS #150-84-5)



Geranyl Aceate (CAS #105-87-3)



Geraniol (CAS #106-24-1)



Nerol (CAS #106-25-2)

Identify Applications/Functional Uses: (EC 2025)
1. Skin conditioning agent - emollient
2. Humectant
3. Fragrance
4. Hair conditioning agent
5. Hair waving or straightening agent

Known Impurities[3]:
No information is available. Polycitronellol acetate is a mixture of short-chain oligomers (P2 Science 2022).

GreenScreen® Summary Rating for Polycitronellol Acetate[4,5 6,7]: Polycitronellol acetate was assigned a **GreenScreen Benchmark™ Score of 2** ("Use but Search for Safer Substitutes") (CPA 2018b). This score is based on the following hazard score combinations:

- Benchmark 2c
  - High Persistence-P + High Ecotoxicity (acute aquatic toxicity-AA)
  - High P + Moderate Ecotoxicity (chronic aquatic toxicity-CA)
  - Very High Persistence-P + Moderate Chronic Aquatic Toxicity-CA

[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 gaps (DG) exist for endocrine activity-E and neurotoxicity (repeated dose)-N (r*). As outlined in GreenScreen® Guidance Section 11.6.2.1 and Annex 5 (Conduct a Data Gap Analysis), polycitronellol acetate meets requirements for a GreenScreen Benchmark™ Score of 2 despite the hazard data gaps. In a worst-case scenario, if polycitronellol acetate 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 Polycitronellol Acetate

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

No data on environmental transformation products were identified for polycitronellol acetate. It is claimed to be biodegradable, and the branching on the oligomer chains is claimed to enhance its biodegradation, but no degradation products were identified (P2 Science 2022). Due to its insolubility, polycitronellol acetate has reduced susceptibility to hydrolysis.

Introduction

Polycitronellol acetate is a low molecular weight liquid polymer that is derived from terpenoids, specifically citronellol (P2 Science 2022). Polycitronellol acetate is obtained by reacting acetic anhydride with the citronellol polymer (EC 2025).

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

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

The SCIL is a list of chemicals that meet the Safer Choice standard (U.S. EPA 2025a). 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 2024).

Polycitronellol acetate is not listed on the U.S. EPA's 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 2025) 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. No pharos output was identified for polycitronellol acetate.

- Polycitronellol acetate is not present in the Pharos database, and therefore a full GreenScreen® is required.
- Polycitronellol acetate is not listed on the U.S. DOT list.

Hazard Statement and Occupational Control

No Globally Harmonized System of Classification and Labelling of Chemicals (GHS) hazard statements were identified for polycitronellol acetate, as indicated in Table 1. General personal protective equipment (PPE) recommendations are presented in Table 2, below. No occupational exposure limits (OELs) were identified.

Table 1: GHS H Statements for Polycitronellol Acetate (CAS #2417284-25-2)
No harmonized GHS H statements are reported by the European Chemicals Agency (ECHA). According to the notifications provided by companies to ECHA in REACH registrations, no hazards have been classified.

Table 2: Occupational Exposure Limits and Recommended Personal Protective Equipment for Polycitronellol Acetate (CAS #2417284-25-2)			
Personal Protective Equipment (PPE)	**Reference**	**Occupational Exposure Limits (OEL)**	**Reference**
Gloves, safety goggles	P2 Science 2020	None identified	

Physicochemical Properties of Polycitronellol Acetate

Polycitronellol acetate is a colorless to light yellow liquid at room temperature. It is not soluble in water and decomposes at temperatures greater than 160°C.

Table 3: Physical and Chemical Properties of Polycitronellol Acetate (CAS #2417284-25-2)		
Property	**Value**	**Reference**
Molecular formula	UVCB	
SMILES Notation	UVCB	
Molecular weight	UVCB	
Physical state	Liquid	P2 Science 2020
Appearance	Colorless to light yellow	P2 Science 2020
Melting point	Not identified	
Boiling point	> 160°C (decomposes)	P2 Science 2022
Vapor pressure	Not identified	
Water solubility	Insoluble in water	P2 Science 2022
Dissociation constant	N/A	
Density/specific gravity	0.89 g/cm^3 at 25°C	P2 Science 2022
Partition coefficient	Not identified	

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

Toxicokinetics
Toxicokinetics data were not identified for polycitronellol acetate.

Hazard Classification Summary

Group I Human Health Effects (Group I Human)

Carcinogenicity (C) Score (H, M, or L): *L*
Polycitronellol acetate was assigned a score of Low for carcinogenicity based on negative results in chronic studies with rodents administered surrogates citronellyl acetate and geranyl acetate. 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 low due to reduced survival of some of the treated groups lowered the sensitivities of these studies.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- NTP 1987
  - *Oral: Surrogate: Citronellyl acetate (CAS #150-84-5) and Geranyl acetate (CAS #105-87-3):* National Toxicology Program (NTP) conducted two chronic cancer bioassays on food grade geranyl acetate, which contains 71% geranyl acetate and 29% citronellyl acetate:
    - The two-year rat study was conducted by administering doses of 1,000 or 2,000 mg/kg via gavage to male and female F344/N rats (50/sex/dose) five times per week for 103 weeks. Squamous cell papillomas in the skin were increased marginally in low dose male rats. The incidence of low dose male rats with either squamous cell papillomas or carcinomas was greater ($P < 0.05$) in comparison with the controls. The historical incidence of squamous cell papillomas or carcinomas (combined) in gavage control male F344/N rats is 3.6% (9/250) at the testing laboratory and 2.5% (25/999) throughout the program. The incidence of all epidermal tumors was not significantly elevated in dosed male rats relative to controls. Under the conditions of the study, food grade geranyl acetate was not carcinogenic for F344/N rats of either sex; however, the reduced survival observed in high dose male rats lowered the sensitivity of the study for detecting neoplastic responses. In male rats, the marginal increases of squamous cell papillomas of the skin and tubular cell adenomas of the kidney may have been related to administration of geranyl acetate.
    - The two-year mouse study was conducted by administering doses of 500 or 1,000 mg/kg via gavage to male and female B6C3F1 mice (50/sex/dose) five times per week for 103 weeks. All high dose male and female mice were dead by week 91 as a result of accidentally being administered 2,800 mg/kg for three days during week 91; survival of low dose and control male mice was comparable. Survival of high-dose male and dosed female mice may have been inadequate for the detection of late-appearing tumors. No evidence of any carcinogenic effect was found in either low or high dose mice of either sex. An infection of the genital tract was probably responsible for the deaths of 14/22 control and 8/32 low dose female mice before the end of the study. Under the condition of this study, food grade geranyl acetate was not carcinogenic for B6C3F1 mice of either sex; however, the reduced survival observed in high dose male mice and high and low dose female mice lowered the sensitivity of these studies for detecting neoplastic responses in these groups.

- NTP concluded that food grade geranyl acetate was not carcinogenic in male or female rats or mice; however, it was noted that the reduced survival observed in high dose male rats, high dose male mice and high and low dose female mice lowered the sensitivity of these studies for detecting neoplastic responses in these groups. Based on this conclusion, citronellyl acetate is not expected to be carcinogenic, either.

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

Polycitronellol acetate was assigned a score of Low for mutagenicity/genotoxicity based on negative weight of evidence for both gene mutations and chromosome aberrations for surrogates citronellyl acetate and geranyl acetate. 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 based on reliable measured data for strong surrogates and conclusions from authoritative bodies.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- P2 Science 2022
  - *In vitro:* Polycitronellol acetate was reported to be not mutagenic in an OECD Guideline 471 bacterial reverse mutation assay. No further details were provided.
  - *In vitro:* Polycitronellol acetate was not reported to be clastogenic in an OECD Guideline 487 *in vitro* micronucleus assay. No further details were provided.
- ECHA CHEM, CAS #150-84-5, 2025
  - *In vitro:* *Surrogate: Citronellyl acetate (CAS #150-84-5):* Citronellyl acetate was not mutagenic in a GLP-compliant OECD Guideline 471 bacterial reverse mutation assay with *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA102 treated at up to 5,000 µg/plate with and without metabolic activation (Klimisch 2, reliable with restrictions).
  - *Surrogate: Geranyl acetate (CAS #105-87-3):* Geranyl acetate was positive for gene mutation in mammalian cells in the presence of metabolic activation in mouse lymphoma cells, but not in human cells. An *in vivo* sex-linked recessive lethal assay in Drosophila indicate that it is not mutagenic *in vivo*. While it was positive for sister chromatid exchange *in vitro* in Chinese hamster ovary (CHO) cells, it was negative for the same effect *in vivo* in mice. Although it was positive for clastogenicity *in vivo* in one non-guideline study in mice, it was negative *in vitro*, and negative in a higher quality study on food grade geranyl acetate *in vivo* in mice. Further, an *in vivo* comet assay was negative. *The overall weight of evidence suggests that geranyl acetate is not genotoxic in vivo.*
- AICIS 2017
  - *Surrogate: Geranyl acetate (CAS #105-87-3):* Both the Joint WHO/FAO Expert Committee on Food Additives (JECFA) and European Food Safety Authority (EFSA) concluded geranyl acetate to be non-genotoxic based on the weight of evidence from available genotoxicity studies.
- Overall, based on results for surrogates citronellyl acetate, and geranyl acetate, and conclusions from JECFA and EFSA on surrogate geranyl acetate, a score of Low was assigned for polycitronellol acetate.

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

Polycitronellol acetate was assigned a score of Low for reproductive toxicity based on a lack reproductive effects in rats administered both oral and dermal doses of surrogate geraniol and nerol in

reproductive / developmental screening assay. GreenScreen® criteria classify chemicals as a Low hazard for reproductive toxicity when adequate negative data are available and they are not GHS classified (CPA 2018b). The confidence in the score is low as it is based on a screening study via the dermal route, which may lead to a lower bioavailability than oral and inhalation routes.

- 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 CHEM, CAS #150-84-5, 2025
  - *Oral: Surrogate: Geraniol (CAS #106-24-1) and Nerol (CAS #106-25-2):* In a GLP-compliant OECD Guideline 421 reproductive / developmental screening assay, Wistar rats (10/sex/group) were administered 0, 100, 300, or 1,000 mg/kg/day a mixture containing 6:4 geraniol and nerol (tradename Geraniol 60) via gavage. Males were exposed for 14 days before mating and 14 days during mating for a minimum of 28 days. Females were exposed for 14 days before mating, 14 days during mating, 22 days of gestation, and at least postnatal day (PND) 4. The authors of the EACH CHEM dossier assigned a reproductive NOAEL of 1,000 mg/kg/day, the highest dose tested, based on the lack of reproductive toxicities observed (Klimisch 1, reliable without restriction).
  - *Dermal: Surrogate: Geraniol (CAS #106-24-1):* The surrogate geraniol was tested in a GLP-compliant reproduction/developmental toxicity screening study according to OECD Guideline 421. Wistar rats (10/sex/dose) were exposed to geraniol on the skin in corn oil at 0, 50, 150, 450 (reduced to 300 after 10 days due to irritation) mg/kg/day, for at least 6 hours daily from 14 days before pairing until gestation day (GD) 19. Parental animals were examined for clinical observation, body weight, food consumption, gross pathology, and histopathology (epididymides, ovaries, skin and testes). Massive skin irritation was observed at 450 mg/kg/day. Less pronounced skin irritation was observed at the mid dose. Slight skin irritation was observed at the low dose in females only. However, no reproductive effects were found. Therefore, the authors established a NOAEL of 300 mg/kg/day for reproductive toxicity, which was the highest dose tested (Klimisch 1, reliable without restriction).

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

Polycitronellol acetate was assigned a score of Low for developmental toxicity based on a lack of specific developmental effects in rats administered oral and dermal doses of surrogates geraniol and nerol. 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 based on reliable measured data for strong surrogates.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA CHEM, CAS #150-84-5, 2025
  - *Oral: Surrogate: Geraniol (CAS #106-24-1) and Nerol (CAS #106-25-2):* In the previously described oral GLP-compliant OECD Guideline 421 reproductive / developmental screening assay, Wistar rats (10/sex/group) were administered 0, 100, 300, or 1,000 mg/kg/day a mixture containing 6:4 geraniol and nerol (tradename Geraniol 60) via gavage. Males were exposed for 14 days before mating and 14 days during mating for a minimum of 28 days. Females were exposed for 14 days before mating, 14 days during mating, 22 days of gestation, and at least PND 4. the authors of the EACH CHEM dossier assigned a parental systemic toxicity NOAEL of 300 mg/kg/day and LOAEL of 1,000 mg/kg/day based on

reduced body weight and body weight gain, and a developmental NOAEL of 100 mg/kg/day and LOAEL of 300 mg/kg/day based on a significantly decreased live birth index at the high dose and significantly decreased pup viability at both the mid and high doses. Study authors attributed the developmental toxicities at the high dose to maternal toxicity. The findings at the mid dose were entirely contributed by one dam, which appeared to be an outlier in the group, with developmental effects judged to be secondary to maternal toxicity as well. Historical control data were not discussed. Therefore, the study authors concluded that the correlation between the toxicity observed in the parental animals and effects seen on the offspring are unclear, with questionable relevance for GHS classification (Klimisch 1, reliable without restriction).

- *Dermal: Surrogate: Geraniol (CAS #106-24-1):* In the previously described GLP-compliant reproduction/developmental toxicity screening study according to OECD Guideline 421 on the surrogate geraniol, Wistar rats (10/sex/dose) were exposed to geraniol on the skin in corn oil at 0, 50, 150, 450 (reduced to 300 after 10 days due to irritation) mg/kg/day, for at least 6 hours daily from 14 days before pairing until GD 19. Litter observations included pup number and status at delivery, pup viability up to post-natal day (PND) 4, sex ratio, clinical observations, body weight, and gross external and visceral examinations. No effects were found on any of these parameters. Therefore, study authors identified a NOAEL of 300 mg/kg/day for developmental toxicity, which was the highest dose tested (Klimisch 1, reliable without restriction).
- *Oral: Surrogate: Geraniol (CAS #106-24-1) and Nerol (CAS #106-25-2):* In a GLP-compliant OECD Guideline 414 prenatal developmental toxicity study, pregnant Wistar rats (25/group) were administered 0, 100, 300, or 1,000 mg/kg/day a mixture containing 6:4 geraniol and nerol (tradename Geraniol 60) via gavage from GD 6 to 19. A significant reduction in pup body weight (9%) was measured at the high dose which was attributed to reduction in maternal food consumption and body weight. The authors of the EACH CHEM dossier assigned a maternal toxicity NOAEL of 100 mg/kg/day and LOAEL of 300 mg/kg/day based on transiently reduced food consumption and body weight gain, and a developmental NOAEL of 300 mg/kg/day and LOAEL of 1,000 mg/kg/day based on reduced fetal body weight (Klimisch 1, reliable without restriction).
- *Oral: Surrogate: Geraniol (CAS #106-24-1):* In a GLP-compliant OECD Guideline 414 prenatal developmental toxicity study, pregnant Wistar rats (25/group) were administered 0, 30, 100, or 300 mg/kg/day geraniol (tradename Geraniol Extra) via gavage from GD 6 to 19. The authors of the EACH CHEM dossier assigned a maternal toxicity and developmental toxicity NOAEL of 300 mg/kg/day based on a lack of adverse effects (Klimisch 1, reliable without restriction).

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

Polycitronellol acetate was assigned a score of Data Gap for endocrine activity based on a lack of sufficient data identified. Surrogate geranyl acetate is mostly negative in high throughput screening assays for estrogen, androgen, steroidogenesis and thyroid pathways. However, there are no *in vivo* data examining circulating hormones or related effects for all endocrine pathways.

- 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 2025b
  - *Surrogate: Geranyl acetate (CAS #105-87-3):* Geranyl acetate was active in 0/18 estrogen receptor (ER) assays, 0/14 androgen receptor (AR) assays, 0/2 steroidogenesis assays, and

1/13 thyroid receptor assays performed as part of the U.S. EPA's Endocrine Disruptor Screening Program (EDSP) in the 21st Century (Appendix C).

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

Polycitronellol acetate was assigned a score of Low for acute toxicity based on oral and dermal LD_{50} values greater than 2,000 mg/kg in rats administered surrogate citronellyl acetate. GreenScreen® criteria classify chemicals as a Low hazard for acute toxicity when adequate data are available and GHS classification is not warranted (CPA 2018b). The confidence in the score is high based on reliable measured data for a strong surrogate.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA CHEM, CAS #150-84-5, 2025
  - *Oral: Surrogate: Citronellyl acetate (CAS #150-84-5):* LD_{50} (Sprague-Dawley rat) = 6,800 mg/kg (Klimisch 2, reliable with restrictions).
  - *Dermal: Surrogate: Citronellyl acetate (CAS #150-84-5):* LD_{50} (New Zealand White rabbit) > 2,000 mg/kg (Klimisch 2, reliable with restrictions).

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

Polycitronellol acetate was assigned a score of Low for systemic toxicity (single dose) based on a lack of specific target organ effects in rats administered a single oral or dermal dose of surrogate citronellyl acetate at or greater than 2,000 mg/kg. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (single dose) when adequate data are available and GHS classification is not warranted (CPA 2018b). The confidence in the score is high based on reliable measured data for a strong surrogate.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA CHEM, CAS #150-84-5, 2025
  - *Oral: Surrogate: Citronellyl acetate (CAS #150-84-5):* In an acute oral toxicity study, Sprague-Dawley rats (2/sex/group) were administered a gavage dose of 0, 3,000, 4,600, 6,800, or 10,200 mg/kg citronellyl acetate and observed for 14 days. Two animals died at 6,800 mg/kg and all animal died at the high dose. No gross pathological findings were observed in sacrificed animals. Clinical signs in surviving animals included hypoactivity, ruffled fur, and muscular weakness. Body weight was measured but results were not reported (Klimisch 2, reliable with restrictions).
  - *Dermal: Surrogate: Citronellyl acetate (CAS #150-84-5):* In an acute dermal toxicity study, New Zealand White rabbits (2/sex) were administered an occlusive application of 2,000 mg/kg citronellyl acetate and observed for 14 days. No deaths occurred, no gross pathological findings were observed, and no clinical signs of toxicity were observed. Body weight was measured but results were not reported (Klimisch 2, reliable with restrictions).

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

Polycitronellol acetate was assigned a score of Low for systemic toxicity (repeated dose) based on NOAELs ≥ 500 mg/kg/day in rats and mice administered repeated oral doses of surrogates citronellyl acetate and geranyl acetate in subchronic and chronic studies. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (repeated dose) when adequate data are available and GHS classification is not warranted (i.e., subchronic LOAELs > 100 mg/kg/day) (CPA 2018b). The confidence in the score is high based on reliable measured data for strong surrogates.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- ECHA CHEM, CAS #150-84-5, 2025
  - *Oral: Surrogate: Citronellyl acetate (CAS #150-84-5) and Geranyl acetate (CAS #105-87-3):* In the previously described NTP chronic toxicity study, Fischer 344 rats (50/sex/group) were administered gavage doses of 29% citronellyl acetate and 71% geranyl acetate at 0, 1,000, or 2,000 mg/kg/day for 103 weeks. Examinations included clinical observations, body weight, gross pathology, and histopathology. Increased mortality was observed in high dose males. Body weight was decreased at the high dose. Incidence of nephropathy was increased in high dose animals, but relation to treatment was not clear to study authors. Overall, the authors of the ECHA CHEM dossier assigned a NOAEL of 1,000 mg/kg/day based on effects observed at the LOAEL of 2,000 mg/kg/day (Klimisch 2, reliable with restrictions).
  - *Oral: Surrogate: Citronellyl acetate (CAS #150-84-5) and Geranyl acetate (CAS #105-87-3):* In the previously described NTP chronic toxicity study, B6C3F1 mice (50/sex/group) were administered gavage doses of 29% citronellyl acetate and 71% geranyl acetate at 0, 500, or 1,000 mg/kg/day for 102 weeks. Examinations included clinical observations, body weight, gross pathology, and histopathology. All high dose animals died at week 91 due to a dosing error. No other treatment-related mortality was observed. Body weight was decrease at the high dose. Increased cytoplasmic vacuolization in the kidney and liver was observed at the high dose (Klimisch 2, reliable with restrictions). *Based on reduced body weight (gain), ToxServices assigned a NOAEL of 500 mg/kg/day and LOAEL of 1,000 mg/kg/day.*
  - *Oral: Surrogate: Citronellyl acetate (CAS #150-84-5) and Geranyl acetate (CAS #105-87-3):* In a NTP subchronic toxicity study, Fischer 344 rats (10/sex/group) were administered gavage doses of 29% citronellyl acetate and 71% geranyl acetate at 0, 250, 500, 1,000, 2,000, or 4,000 mg/kg/day for 13 weeks. Examinations included clinical observations, body weight, gross pathology, and histopathology. A slight increase in mortality was observed at the high dose. Body weight was decreased at the high dose. Reddening of the stomach was observed in some high dose males. The authors of the ECHA CHEM dossier assigned a NOAEL of 2,000 mg/kg/day and LOAEL of 4,000 mg/kg/day based on reduced body weight (Klimisch 2, reliable with restrictions).
  - *Oral: Surrogate: Citronellyl acetate (CAS #150-84-5) and Geranyl acetate (CAS #105-87-3):* In a NTP subchronic toxicity study, B6C3F1 mice (10/sex/group) were administered gavage doses of 29% citronellyl acetate and 71% geranyl acetate at 0, 125, 250, 500, 1,000, or 2,000 mg/kg/day for 13 weeks. Examinations included clinical observations, body weight, gross pathology, and histopathology. A significant increase in mortality was observed at the high dose. Body weight development was slightly delayed at the high dose. Increased cytoplasmic vacuolization in the kidney and liver was observed at the high dose along with inflammation of the stomach. The authors of the ECHA CHEM dossier assigned

a NOAEL of 1,000 and LOAEL of 2,000 mg/kg/day based on increased mortality, delayed body weight gain, and kidney pathological findings (Klimisch 2, reliable with restrictions).

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

Polycitronellol acetate was assigned a score of Low for neurotoxicity (single dose) based on a lack of specific neurotoxic effects in rats administered a single oral or dermal dose of surrogate citronellyl acetate at or greater than 2,000 mg/kg. GreenScreen® criteria classify chemicals as a Low hazard for neurotoxicity (single dose) when adequate data are available and GHS classification is not warranted (CPA 2018b). The confidence in the score is low as there were no specific neurotoxicity examinations.

- 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 CHEM, CAS #150-84-5, 2025
  - *Oral:* *Surrogate: Citronellyl acetate (CAS #150-84-5):* In an acute oral toxicity study, Sprague-Dawley rats (2/sex/group) were administered a gavage dose of 0, 3,000, 4,600, 6,800, or 10,200 mg/kg citronellyl acetate and observed for 14 days. Two animals died at 6,800 mg/kg and all animal died at the high dose. No gross pathological findings were observed in sacrificed animals. Clinical signs in surviving animals included hypoactivity (≥ 3,000 mg/kg), ruffled fur (≥ 4,600 mg/kg), and muscular weakness (≥ 4,600 mg/kg). The reversibility of these effects were not reported (Klimisch 2, reliable with restrictions). *Hypoactivity and muscular weakness may be signs of narcotic effects, but may also reflect general toxicity as these effect occurred at high doses (higher than GHS Category 2 cutoff of 2,000 mg/kg), therefore, ToxServices did not consider them sufficient for GHS Category 3 (transient narcotic effects) classification.*
  - *Dermal:* *Surrogate: Citronellyl acetate (CAS #150-84-5):* In an acute dermal toxicity study, New Zealand White rabbits (2/sex) were administered an occlusive application of 2,000 mg/kg citronellyl acetate and observed for 14 days. No deaths occurred, no gross pathological findings were observed, and no clinical signs of toxicity were observed (Klimisch 2, reliable with restrictions).

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

Polycitronellol acetate was assigned a score of Data Gap for neurotoxicity (repeated dose) based on a lack of data 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.
- No data were identified.

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

Polycitronellol acetate was assigned a score of Low for skin sensitization based on three negative *in vitro* / *in silico* assays for itself with limited details, and less than 15% population response in a non-adjuvant Buehler test with surrogate citronellyl acetate. GreenScreen® criteria classify chemicals as a Low hazard for skin sensitization when adequate data are available and GHS classification is not warranted (CPA 2018b). The confidence in the score is high based on reliable measured data for a strong surrogate.

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

- P2 Science 2022
  - *In vitro:* Polycitronellol acetate was reported to be negative in an OECD Guideline 442D direct peptide reactivity assay. No further details were provided.
  - *In vitro:* Polycitronellol acetate was reported to be negative in an OECD Guideline 442C human cell line activation assay. No further details were provided.
  - *In vitro:* Polycitronellol acetate was reported to be negative in an OECD Guideline 442E KeratinoSens assay. No further details were provided.
- ECHA CHEM, CAS #150-84-5, 2025
  - *Surrogate: Citronellyl acetate (CAS #150-84-5):* Citronellyl acetate was not sensitizing in a GLP-compliant Buehler test conducted according to OECD Guideline 406 with female Dunkin-Hartley guinea pigs (n=20) induced epicutaneously with 100% test substance and challenged epicutaneously 100% test substance. A reaction was reported in one animal at the 24-hour observation, and no reactions were observed at 48 hours (Klimisch 1, reliable without restriction).
    - *Based on the less than 15% population response, GHS Category 1 classification is not warranted.*

Respiratory Sensitization (SnR) (Group II*) Score (H, M, or L): *L*
Polycitronellol acetate was assigned a score of Low for respiratory sensitization based on the lack of dermal sensitization potential, lack of structural alerts for respiratory sensitization, and 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). Confidence in the score is low as this evaluation does not include non-immunologic mechanisms of respiratory sensitization, and no specific data are available for respiratory sensitization.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- OECD 2024
  - *Surrogate: Citronellyl acetate (CAS #150-84-5):* Citronellyl acetate 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 surrogate citronellyl acetate 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 polycitronellol acetate, and as surrogate/building block citronellyl acetate does not contain any structural alerts for respiratory sensitization (OECD 2024), polycitronellol acetate is not expected to be a respiratory sensitizer.

Skin Irritation/Corrosivity (IrS) (Group II) Score (vH, H, M, or L): *L*
Polycitronellol acetate was assigned a score of Low for skin irritation/corrosivity based on a negative *in vitro* skin irritation study conducted according to OECD Guideline 439 for the target chemical. GreenScreen® criteria classify chemicals as a Low hazard for skin irritation/corrosivity when adequate data are available and they are not classified under GHS (CPA 2018b). The confidence in the score is

low due to limited reporting of the study, and that the OECD Guideline 439 test does not differentiate between GHS Category 3 (GreenScreen® Moderate) and GHS not classified (GreenScreen® Low).

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- P2 Science 2022
  - *In vitro:* Polycitronellol acetate was reported to be negative in an OECD Guideline 439 EpiDerm™ skin irritation assay. No further details were provided.
    - *The OECD Guideline 439 is intended to identify GHS Category 2 irritants. The negative results in this assay indicate that the test substance is not GHS Category 3. However, it does not inform on whether the substance is classifiable to GHS Category 3 (OECD 2021).*
- ECHA CHEM, CAS #150-84-5, 2025
  - *Surrogate: Citronellyl acetate (CAS #150-84-5):* In a GLP-compliant skin irritation study conducted according to OECD Guideline 404, New-Zealand White rabbits (n=3) were treated with 0.5 mL of undiluted citronellyl acetate on shaved skin for 4 hours under semi-occlusive conditions. Animals were observed for 15 days. The individual mean 24/48/72-hour erythema scores were 3, 2.33, and 2.33, and the individual mean 24/48/72-hour edema scores were 1, 0.67, and 0.67. Effects were reversible within 15 days (Klimisch 1, reliable without restriction).
    - *Based on individual erythema scores of greater than 2.3 in all three animals, a GHS Category 2 classification is warranted.*
- Based on the weight of evidence, a score of Low was assigned. The surrogate citronellyl acetate is a GHS Category 2 skin irritant in rabbits. However, the surrogate is significantly smaller than polycitronellol acetate and is a conservative surrogate. Therefore, ToxServices weighed the data on polycitronellol acetate itself more heavily, even though it had limited reporting.

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

Polycitronellol acetate was assigned a score of Low for eye irritation/corrosivity based on negative results in eye irritation studies *in vitro* with the target substance, and in rabbits administered surrogate citronellyl acetate. GreenScreen® criteria classify chemicals as a Low hazard for eye irritation/corrosivity when GHS classification is not warranted (CPA 2018b). The confidence in the score is high based on reliable measured data for a strong surrogate.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- P2 Science 2022
  - *In vitro:* Polycitronellol acetate was reported to be negative in an OECD Guideline 437 bovine corneal opacity and permeability test. No further details were provided.
- ECHA CHEM, CAS #150-84-5, 2025
  - *Surrogate: Citronellyl acetate (CAS #150-84-5):* In a GLP-compliant eye irritation study conducted according to OECD Guideline 405, New-Zealand White rabbits (n=3) were instilled with 0.1 mL of undiluted citronellyl acetate in the eye. Animals were observed for 72 hours. The individual mean 24/48/72-hour iris, chemosis, conjunctiva, and corneal opacity scores were zero for all animals (Klimisch 1, reliable without restriction).

Ecotoxicity (Ecotox)

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

Polycitronellol acetate was assigned a score of High for acute aquatic toxicity based on L/EC_{50} values between 1 and 10 mg/L in fish, daphnid, and algae exposed to surrogate citronellyl acetate. GreenScreen® criteria classify chemicals as a High hazard for acute aquatic toxicity when L/EC_{50} values are between 1 and 10 mg/L in fish, daphnid, and algae (CPA 2018b). The confidence in the score is low as it is based on reliable measured data for a conservative surrogate that may be more toxic than the target substance.

- 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 CHEM, CAS #150-84-5, 2025
  - *Surrogate: Citronellyl acetate (CAS #150-84-5):* 96-hour LC_{50} (*Danio rerio*, zebrafish) = 6.1 mg/L (GLP, OECD Guideline 203) (Klimisch 1, reliable without restriction).
  - *Surrogate: Citronellyl acetate (CAS #150-84-5):* 48-hour mobility EC_{50} (*Daphnia magna*) = 3.48 mg/L (GLP, OECD Guideline 202) (Klimisch 1, reliable without restriction).
  - *Surrogate: Citronellyl acetate (CAS #150-84-5):* 72-hour growth rate EC_{50} (*Desmodesmus subspicatus*) > 7.2 mg/L (GLP, OECD Guideline 202) (Klimisch 2, reliable with restrictions).

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

Polycitronellol acetate was assigned a score of Moderate for chronic aquatic toxicity based on an experimental 72-hour growth rate NOEC of 2.22 mg/L for algae. GreenScreen® criteria classify chemicals as a Moderate hazard for chronic aquatic toxicity when chronic values are between 1 and 10 mg/L (CPA 2018b). The confidence in the score is low as data were not identified for the fish and crustacea 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 CHEM, CAS #150-84-5, 2025
  - *Surrogate: Citronellyl acetate (CAS #150-84-5):* 72-hour growth rate NOEC (*D. subspicatus*) = 2.22 mg/L (GLP, OECD Guideline 202) (Klimisch 2, reliable with restrictions).
- U.S. EPA 2022
  - *Surrogate: Citronellyl acetate (CAS #150-84-5):* Citronellyl acetate is designated to the Esters and Neutral Organics ECOSAR chemical classes. The most conservative ChVs are 0.06 mg/L in fish, 0.111 mg/L in daphnia, and 0.158 mg/L in green algae (Appendix E).
- Based on the weight of evidence, a score of Moderate was assigned. No measured data were identified for surrogate citronellyl acetate for fish and daphnia trophic levels. The modeled data for fish indicate a Very High score (< 0.1 mg/L), and the modeled data for daphnia indicate a High score (0.1-1 mg/L). However, the modeled data in algae of 0.158 mg/L is one order of magnitude lower than the experimental value of 2.2 mg/L. Additionally, measured acute toxicity data indicate the toxicities to all three trophic levels are of similar orders of magnitude. Therefore, ToxServices did not rely on modeled data to score this endpoint.

Environmental Fate (Fate)

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

Polycitronellol acetate was assigned a score of High for persistence based on being inherently biodegradable in an OECD Guideline 301B test, along with estimated data indicating it has a half-life of 542 days in its predicted major compartment, sediment. GreenScreen® criteria classify chemicals as a High hazard for persistence when soil and sediment are the dominant environmental compartment with a half-life of 60-180 days (CPA 2018b). The confidence in the score is low as it is based on expert judgment and there are no measured half-life data in the dominant environmental compartment, sediment.

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- P2 Science 2022
  - Polycitronellol acetate was reported to be inherently biodegradable in an OECD Guideline 301 B biodegradability test. No further details were provided.
- P2 Science Undated
  - Polycitronellol acetate under the tradename Citropol® HA was inherently biodegradable in an OECD Guideline 301B biodegradability test. Based on the degradation curve presented, Citropol® HA achieved approximately 55% degradation in 28 days.
- ECHA CHEM, CAS #150-84-5, 2025
  - *Surrogate: Citronellyl acetate (CAS #150-84-5):* Citronellyl acetate was readily biodegradable in a biodegradation assay conducted according to OECD Guideline 310 (Ready Biodegradability - CO2 in Sealed Vessels (Headspace Test). In this assay, domestic, non-adapted, activated sludge was exposed to the test substance at 30 mg/L for 28 days. A biodegradation rate of 93% was achieved at the end of the exposure period. A biodegradation rate of 76% was achieved during the 10-day window, and the compound therefore met the 10-day window (Klimisch 1, reliable without restriction).
- U.S. EPA 2017
  - Using a representative structure of polycitronellol acetate where n=2, the following prediction results were obtained:
  - BIOWIN modeling predicts that the substance is not readily biodegradable. Level III Fugacity modeling (EQC default) predicts 68.7% will partition to sediment with a half-life of 541.67 days, 29.9% to soil with a half-life of 120 days, and 1.39% to water with a half-life of 60 days (Appendix D).
- Based on the weight of evidence, a score of High is assigned for polycitronellol acetate. Although a representative structure with a relatively short chain length was predicted to have a half-life of 542 days in its major compartment, sediment, which warrants a Very High score, polycitronellol acetate was reported to be inherently biodegradable in an OECD Guideline 301 B study and monomer citronellyl acetate was readily biodegradable in an OECD Guideline 310 ready degradability test. Therefore, ToxServices did not consider polycitronellol acetate to be recalcitrant (Very High). Although the OECD Guideline 301B ready biodegradability test on the target chemical indicates a half-life of < 28 days which is within the 16-40 days range for a Moderate score in water, EPI Suite™ predicts that water is not a major compartment for polycitronellol acetate, and hence half-lives in water could not be used to score this endpoint when the target chemical is not rapidly or readily biodegradable. EPI Suite™ predicted a half-life of 60 days in water, which is more conservative than the measured half-life (i.e., < 28 days) in water. Therefore, it is likely that the

predicted half-life in sediment (the predicted major compartment) of 542 days is also conservative. As a result, ToxServices assigned a High score instead of Very High score for this endpoint.

Bioaccumulation (B) Score (vH, H, M, L, or vL): *L*
Polycitronellol acetate was assigned a score of Low for bioaccumulation based on an estimated BAF value of 240 for a constituent with n=2. GreenScreen® criteria classify chemicals as a Low hazard for bioaccumulation when BAF values are between 100 and 500 (CPA 2018b). The confidence in the score is low based on the 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.
- U.S. EPA 2017
  - Using a representative structure of polycitronellol acetate where n=2, the following prediction results were obtained:
  - BCFBAF predicts a BAF of 240.4 using the Arnot-Gobas method for the upper trophic level, based on an estimated log K_{ow} of 11.5 (Appendix F).

Physical Hazards (Physical)

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

- Authoritative and Screening Lists
  - *Authoritative:* Not present on any authoritative lists for this endpoint.
  - *Screening:* Not present on any screening lists for this endpoint.
- No measured data were identified. Therefore, screening procedures for explosivity were used here to estimate the reactivity property of polycitronellol acetate. These procedures are listed in the GHS (UN 2023).
  - Based on the structure of its components or moieties, Polycitronellol acetate 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, polycitronellol acetate is not considered to have oxidizing properties as it does not contain any structural groups known to be correlated with a tendency to react exothermally with combustible materials. Specifically, organic substances which contain oxygen, fluorine, or chlorine where these elements are chemically bonded only to carbon or hydrogen, classification as an oxidizing liquid need not be applied. Therefore, as the molecular structure of polycitronellol acetate has oxygens which are all bonded only to carbon and hydrogen, classification is not warranted.

Flammability (F) Score (vH, H, M, or L): L
Polycitronellol acetate was assigned a score of Low for flammability based on a flash point of > 150°C, which is above the guidance value of 93°C for GHS Category 4 flammable liquids. GreenScreen® criteria classify chemicals as a Low hazard for flammability when GHS classification is not warranted (CPA 2018b). The confidence in the score is high based on data for the target chemical.

- Authoritative and Screening Lists
    - *Authoritative:* Not present on any authoritative lists for this endpoint.
    - *Screening:* Not present on any screening lists for this endpoint.
- P2 Science 2020
    - Polycitronellol acetate has a flash point of > 150°C.
        - *According to GHS criteria (UN 2023), the flash point of > 150°C is above the guidance value of 93°C for Category 4 flammable liquids, therefore GHS classification is not warranted.*

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

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

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

As shown in Table 4, Type I (input data) uncertainties in polycitronellol acetate's NAMs dataset include absence of, or inadequate experimental data for endocrine activity, skin sensitization, respiratory sensitization, skin and eye irritation, chronic aquatic toxicity, and bioaccumulation, and lack of established test methods for respiratory sensitization. Polycitronellol acetate's Type II (extrapolation output) uncertainties include limitations of *in vitro* genotoxicity assays to mimic *in vivo* metabolic conditions and their focusing on a few genotoxicity events, incomplete coverage of EDSP Tox 21 assays of critical endocrine pathways ant their uncertain *in vivo* relevance, the inability of *in vitro* skin sensitization assays in evaluating pro-haptens and pre-haptens, lack of defined applicability domains of the OECD Toolbox structural alerts for respiratory sensitization, and its lack of consideration of non-immunological mechanisms of respiratory sensitization, limitations of *in vitro* skin and eye irritation assays in determining single GHS classifications, and the inaccurate prediction of aquatic toxicities for this type of substances. Some of polycitronellol acetate's type II uncertainties were alleviated by the use of *in vitro* test batteries and/or in combination of *in vivo* data.

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

Uncertainty Analyses (OECD 2020)	
Type I Uncertainty: Data/Model Input	**Genotoxicity:** No Type I uncertainty is identified on using the *in vitro* genotoxicity assays as they are considered relevant (appropriate for the evaluation of the corresponding hazards as recommended in the OECD Guideline), reliable (they have Klimisch scoring of 2 or 1) and adequate (validated methods). **Endocrine activity:** No *in vivo* data are available. **Skin sensitization:** No *in vivo* data are available for the target substance.

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

	Respiratory sensitization: No experimental data are available and there are no validated test methods. **Skin and eye irritation:** No *in vivo* experimental data are available for the test substance. **Chronic aquatic toxicity:** No measured data are available for the fish and daphnia trophic levels. **Bioaccumulation:** No experimental data are available.
Type II Uncertainty: Extrapolation Output	**Genotoxicity:** The bacterial reverse mutation assay (as defined in OECD Guideline 471) only tests point-mutation inducing activity in non-mammalian cells, and the exogenous metabolic activation system does not entirely mimic *in vivo* conditions[10]. The mammalian cell gene mutation assay (as defined in OECD Guideline 476) only detects gene mutations, and the exogenous metabolic activation system does not entirely mirror *in vivo* metabolism (i.e., the liver S9 mix contains enzymes present in the endoplasmic reticulum but not the cytosol of liver cells).[11] The *in vitro* chromosome aberration assay (OECD Guideline 473) does not measure aneuploidy and it only measures structural chromosomal aberrations. The exogenous metabolic activation system does not entirely mirror *in vivo* metabolism[12]. The *in vitro* SCE assay (as defined in OECD Guideline 479, a guideline deleted in 2014) detects reciprocal exchange of DNA without providing the underlying mechanism of action[13]. **Endocrine activity:** The *in vivo* relevance of EDSP Tox 21 screening assays is unknown due to lack of consideration of metabolism and other toxicokinetic factors. EDSP Tox 21 assays do not cover all critical endocrine pathways. **Skin sensitization:** The *in silico* and *in vitro* assays evaluating key events in the skin sensitization adverse outcome pathway (AOP) don't typically include metabolism or abiotic transformation to address chemicals that are pro-haptens or pre-haptens, respectively.

[10] https://www.oecd-ilibrary.org/docserver/9789264071247-en.pdf?expires=1614097593&id=id&accname=guest&checksum=89925F80B9F4BD2FFC6E90F94A0EE427
[11] https://www.oecd-ilibrary.org/docserver/9789264264809-en.pdf?expires=1614097800&id=id&accname=guest&checksum=C0DE371FB9C5A878E66C9AB7F84E6BBE
[12] https://www.oecd-ilibrary.org/docserver/9789264264649-en.pdf?expires=1614098015&id=id&accname=guest&checksum=6A4F9CE52EA974F5A74793DD54D54352
[13] https://www.oecd.org/env/ehs/testing/Draft_Intro_Genotoxicity%20TGs%20September%202014.pdf

	Further, each test has their applicable domain such as limitations in test substance solubility or log K_{ow}.[14] **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. **Skin irritation:** The OECD Guideline 439 test is only used to identify irritating substances (GHS Category 2) and non-irritating substances (no category), and does not allow the classification as a mild skin irritant (GHS Category 3)[15]. **Eye irritation:** The BCOP (OECD Guideline 437) test is not recommended for identifying GHS Category 2A or 2B irritants[16]. **Chronic aquatic toxicity:** The modeled values are much lower than experimental data.	
Endpoint	**NAMs Data Available and Evaluated? (Y/N)**	**Types of NAMs Data (*in silico* modeling/*in vitro* biological profiling/frameworks)**
Carcinogenicity	N	
Mutagenicity	Y	*In vitro* data: Bacterial reverse mutation assay/*in vitro* gene mutation assay/*in vitro* sister chromatid exchange assay/ *in vitro* chromosomal aberration assay
Reproductive toxicity	N	
Developmental toxicity	N	
Endocrine activity	Y	*In vitro* high throughput data: EDSP Tox 21 screening assays
Acute mammalian toxicity	N	
Single exposure systemic toxicity	N	
Repeated exposure systemic toxicity	N	
Single exposure neurotoxicity	N	
Repeated exposure neurotoxicity	N	

[14] https://www.oecd-ilibrary.org/environment/test-no-442c-in-chemico-skin-sensitisation_9789264229709-en; https://www.oecd-ilibrary.org/environment/test-no-442d-in-vitro-skin-sensitisation_9789264229822-en; https://www.oecd-ilibrary.org/environment/test-no-442e-in-vitro-skin-sensitisation_9789264264359-en
[15] https://www.oecd-ilibrary.org/docserver/9789264242845-en.pdf?expires=1614097324&id=id&accname=guest&checksum=D664A7EDCDE297919BE9A478941EBEC6
[16] https://www.oecd-ilibrary.org/docserver/9789264203846-en.pdf?expires=1614095760&id=id&accname=guest&checksum=1613168F64BDB3558225572BDD75FC8D

Skin sensitization	Y	*In vitro* data: OECD Guideline 442C, D, and E assays
Respiratory sensitization	Y	*In silico* modeling: OECD Toolbox structural alerts
Skin irritation	Y	*In vitro* data: OECD Guideline 439 EpiDerm™ skin irritation assay
Eye irritation	Y	*In vitro* data: OECD Guideline 437 bovine corneal opacity and permeability test
Acute aquatic toxicity	N	
Chronic aquatic toxicity	Y	*In silico* modeling: ECOSAR
Persistence	Y	Non-animal testing: OECD Guideline 301 Biodegradation tests *In silico* modeling: EPI Suite™
Bioaccumulation	Y	*In silico* modeling: EPI Suite™

References

Australian Industrial Chemicals Introduction Scheme (AICIS). 2017. Simple esters of geraniol and nerol: human health tier II assessment. IMAP Group Assessment Report. Available: https://www.industrialchemicals.gov.au/sites/default/files/Simple%20esters%20of%20geraniol%20and%20nerol_Human%20health%20tier%20II%20assessment.pdf

Clean Production Action (CPA). 2018a. GreenScreen® Assessment Expiration Policy. October 2, 2018.

Clean Production Action (CPA). 2018b. The GreenScreen® for Safer Chemicals Guidance. Version 1.4 Guidance. Dated January, 2018. Available: https://www.greenscreenchemicals.org/static/ee_images/uploads/resources/GreenScreen_Guidance_v1_4_2018_01_Final.pdf

European Chemicals Agency (ECHA). 2017. Guidance on information requirements and Chemical Safety Assessment. Chapter R.7a: Endpoint specific guidance. Version 6.0. Dated: July 2017. Available: https://echa.europa.eu/documents/10162/17224/information_requirements_r7a_en.pdf/e4a2a18f-a2bd-4a04-ac6d-0ea425b2567f?t=1500286622893

European Chemicals Agency Chemicals Database (ECHA CHEM). 2025. Information on chemicals. Available: https://chem.echa.europa.eu/

European Commission (EC). 2025. CosIng Database. Available: https://ec.europa.eu/growth/tools-databases/cosing/advanced

European Food Safety Authority (EFSA). 2018. Guidance on uncertainty analysis in scientific assessments. *EFSA J.* 16(1): e05123. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7009727/

Madden, J.C., S.J. Enoch, A. Paini, and M.T.D. Cronin. 2020. A review of *in silico* tools as alternatives to animal testing: principles, resources, and applications. *Alt. Lab. Animals.* 1-27. Available: https://journals.sagepub.com/doi/pdf/10.1177/0261192920965977

National Toxicology Program (NTP). 1987. Carcinogenesis Studies of Food Grade Geranyl Acetate (71% Geranyl Acetate, 29% Citronellyl Acetate) (CAS No. 105-87-3) in F344/N Rats and B6C3F$_1$ Mice (Gavage Study). Report date October 1987. Available: https://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr252.pdf?utm_source=direct&utm_medium=prod&utm_campaign=ntpgolinks&utm_term=tr252

Organisation for Economic Co-operation and Development (OECD). 2020. Overview of Concepts and Available Guidance related to Integrated Approaches to Testing and Assessment (IATA), Series on Testing and Assessment, No. 329, Environment, Health and Safety, Environment Directorate. Available: https://www.oecd.org/chemicalsafety/risk-assessment/concepts-and-available-guidance-related-to-integrated-approaches-to-testing-and-assessment.pdf

Organisation for Economic Co-operation and Development (OECD). 2021. Test Guideline No. 439. *In vitro* skin irritation: reconstructed human epidermis test methods. June 14, 2021. Available: https://www.oecd.org/en/publications/2021/06/test-no-439-in-vitro-skin-irritation-reconstructed-human-epidermis-test-method_g1g59b2f.html

Organisation for Economic Co-operation and Development (OECD). 2024. OECD QSAR Toolbox for Grouping Chemicals into Categories Version 4.7. Available: https://www.oecd.org/chemicalsafety/risk-assessment/oecd-qsar-toolbox.htm#Download_qsar_application_toolbox

P2 Science. 2020. Safety data sheet for Citropol® 1A. Dated October 19, 2020. Available: https://p2science.com/wp-content/uploads/2021/09/MSDS-Citropol-1A.pdf

P2 Science. 2022. Citropol® Book. Available: https://p2science.com/wp-content/uploads/2022/04/Citropol-Book-2022.pdf

P2 Science. Undated. Citropol® HA product sheet. Available: https://p2science.com/wp-content/uploads/2021/09/P2-Science-Citropol®-HA-Product-Sheet.pdf

Pharos. 2025. Pharos chemical and material library entry for Polycitronellol acetate (CAS #2417284-25-2). Available: http://www.pharosproject.net/material/.

ToxServices. 2021. SOP 1.37: GreenScreen® Hazard Assessments. Dated: May 24, 2021.

United Nations (UN). 2023. Globally Harmonized System of Classification and Labelling of Chemicals (GHS). Tenth revised edition.

United States Department of Transportation (U.S. DOT). 2008a. Chemicals Listed with Classification. 49 CFR § 172.101. Available: http://www.gpo.gov/fdsys/pkg/CFR-2008-title49-vol2/pdf/CFR-2008-title49-vol2-sec172-101.pdf.

United States Department of Transportation (U.S. DOT). 2008b. Classification Criteria. 49 CFR § 173. Available: http://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&tpl=/ecfrbrowse/Title49/49cfr173_main_02.tpl

United States Environmental Protection Agency (U.S. EPA). 2017. Estimation Programs Interface (EPI) Suite™ Web, v4.11, Washington, DC, USA. Available: http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm.

United States Environmental Protection Agency (U.S. EPA). 2020. New Approach Methods Workplan. Office of Research and Development. Office of Chemical Safety and Pollution Prevention. EPA 615B20001. June 2020. Available: https://www.epa.gov/sites/default/files/2020-06/documents/epa_nam_work_plan.pdf

United States Environmental Protection Agency (U.S. EPA). 2022. ECOSAR 2.2. Washington, DC, USA. Available: http://www.epa.gov/oppt/newchems/tools/21ecosar.htm/.

United States Environmental Protection Agency (U.S. EPA). 2024. EPA's Safer Choice and Design for the Environment (DfE) Standard. Available: https://www.epa.gov/saferchoice/standard

United States Environmental Protection Agency (U.S. EPA). 2025a. Safer Chemical Ingredients List (SCIL). Available: https://www.epa.gov/saferchoice/safer-ingredients

United States Environmental Protection Agency (U.S. EPA). 2025b. CompTox database. Available: https://comptox.epa.gov/dashboard/chemical/invitrodb/DTXSID0020654

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 Polycitronellol Acetate (CAS #2417284-25-2)

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	Polycitronellol acetate	2417284-25-2	*L*	L	*L*	L	DG	L	L	L	*L*	DG	L	*L*	*L*	L	*H*	*M*	*H*	*L*	*L*	L

Table 3: Hazard Summary Table

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

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
Polycitronellol acetate	2

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

Table 6

Chemical Name	Final GreenScreen® Benchmark Score
Polycitronellol acetate	2

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

Table 5: Data Gap Assessment Table

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

APPENDIX C: Tox 21 EDSP Assay Results for Geranyl Acetate (CAS #105-87-3)

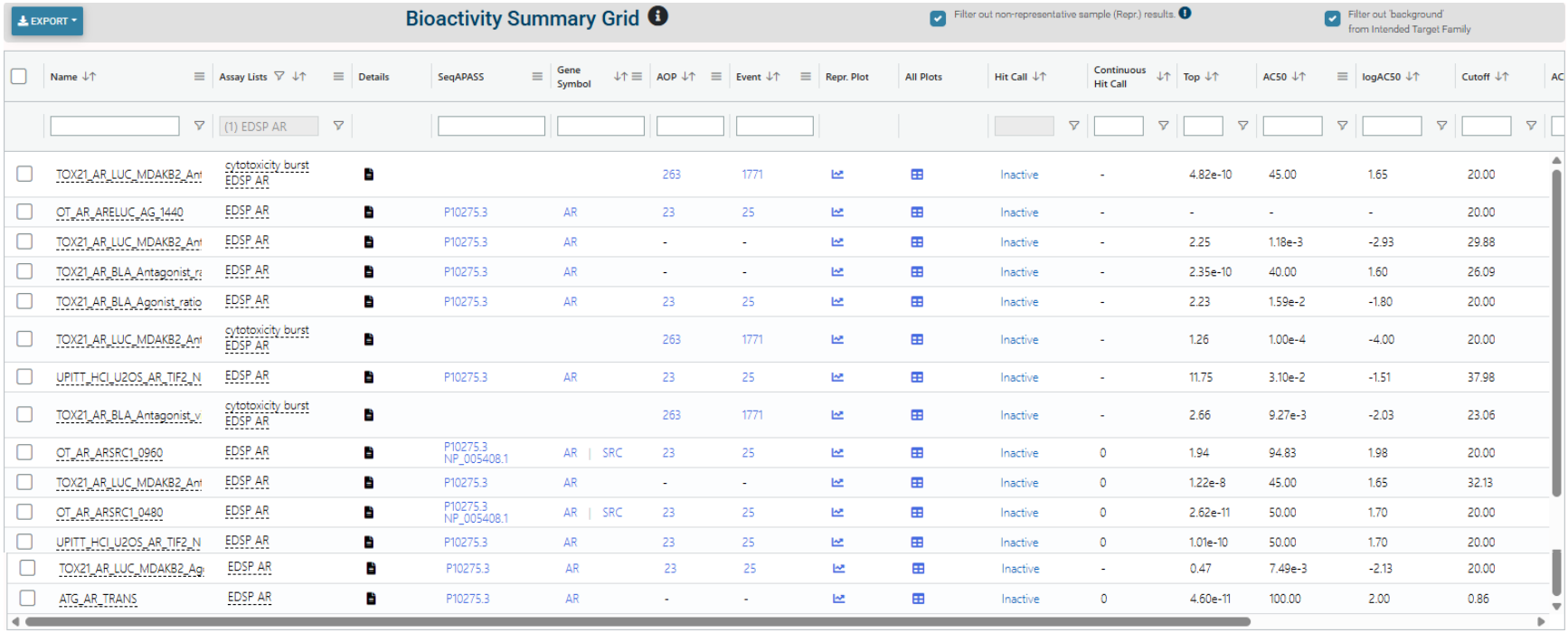
EXPORT

Bioactivity Summary Grid

Filter out non-representative sample (Repr.) results

Filter out 'background' from Intended Target Family

Name	Assay Lists	Details	SeqAPASS	Gene Symbol	AOP	Event	Repr. Plot	All Plots	Hit Call	Continuous Hit Call	Top	AC50	logAC50	Cutoff	AC
	(1) EDSP ER														
ATG_ERa_TRANS	EDSP ER		NP_000116.2	ESR1	-	-			Inactive	0	0.67	7.80	0.89	1.10	
TOX21_ERa_BLA_Antagonist_	EDSP ER cytotoxicity burst				263	1771			Inactive	-	1.87	4.71e-2	-1.33	38.89	
OT_ER_ERbERb_0480	EDSP ER		NP_001428.1	ESR2	-	-			Inactive	-	0.59	50.00	1.70	20.00	
OT_ER_ERaERa_0480	EDSP ER		NP_000116.2	ESR1	-	-			Inactive	-	3.19e-11	50.00	1.70	20.00	
ACEA_ER_80hr	EDSP ER		NP_000116.2	ESR1	220	1394			Inactive	0	2.12	50.00	1.70	25.49	
TOX21_ERa_BLA_Antagonist_	EDSP ER		NP_000116.2	ESR1	-	-			Inactive	-	0.83	3.38e-3	-2.47	20.00	
TOX21_ERa_LUC_VM7_Antag	cytotoxicity burst EDSP ER				263	1771			Inactive	-	3.00e-10	45.00	1.65	24.57	
OT_ER_ERaERb_1440	EDSP ER		NP_000116.2 NP_001428.1	ESR1 | ESR2	-	-			Inactive	-	1.33e-10	50.00	1.70	20.00	
OT_ERa_GFPERaERE_0120	EDSP ER		NP_000116.2	ESR1	-	-			Inactive	0	6.57	50.00	1.70	20.00	
OT_ER_ERaERa_1440	EDSP ER		NP_000116.2	ESR1	-	-			Inactive	-	7.39e-12	50.00	1.70	20.00	
TOX21_ERa_BLA_Agonist_rati	EDSP ER		NP_000116.2	ESR1	-	-			Inactive	-	1.76	40.00	1.60	20.00	
ATG_ERE_CIS	EDSP ER		NP_000116.2	ESR1	-	-			Inactive	0.0127	0.48	65.58	1.82	0.50	
OT_ERa_GFPERaERE_0480	EDSP ER		NP_000116.2	ESR1	-	-			Inactive	-	1.22e-11	50.00	1.70	20.00	
TOX21_ERa_LUC_VM7_Antag	EDSP ER		NP_000116.2	ESR1	-	-			Inactive	-	1.89	0.16	-0.80	24.50	
TOX21_ERa_LUC_VM7_Agoni	EDSP ER		NP_000116.2	ESR1	-	-			Inactive	0	9.07	45.00	1.65	20.00	
OT_ER_ERbERb_1440	EDSP ER		NP_001428.1	ESR2	-	-			Inactive	-	1.00e-10	50.00	1.70	20.00	
ACEA_ER_AUC_viability	cytotoxicity burst EDSP ER				220 | 263	1394 | 1821			Inactive	0	6.18	1.29e-2	-1.89	20.00	
OT_ER_ERaERb_0480	EDSP ER		NP_000116.2 NP_001428.1	ESR1 | ESR2	-	-			Inactive	-	-	-	-	23.30	



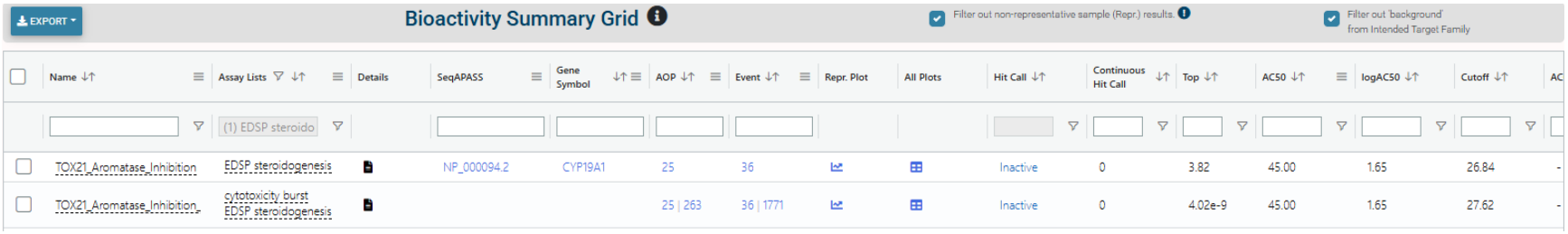
EXPORT

Bioactivity Summary Grid

Filter out non-representative sample (Repr.) results

Filter out 'background' from Intended Target Family

Name	Assay Lists	Details	SeqAPASS	Gene Symbol	AOP	Event	Repr. Plot	All Plots	Hit Call	Continuous Hit Call	Top	AC50	logAC50	Cutoff	AC
	(1) EDSP AR														
TOX21_AR_LUC_MDAKB2_Ant	cytotoxicity burst EDSP AR				263	1771			Inactive	-	4.82e-10	45.00	1.65	20.00	
OT_AR_ARELUC_AG_1440	EDSP AR		P10275.3	AR	23	25			Inactive	-	-	-	-	20.00	
TOX21_AR_LUC_MDAKB2_Ant	EDSP AR		P10275.3	AR	-	-			Inactive	-	2.25	1.18e-3	-2.93	29.88	
TOX21_AR_BLA_Antagonist_r	EDSP AR		P10275.3	AR	-	-			Inactive	-	2.35e-10	40.00	1.60	26.09	
TOX21_AR_BLA_Agonist_ratio	EDSP AR		P10275.3	AR	23	25			Inactive	-	2.23	1.59e-2	-1.80	20.00	
TOX21_AR_LUC_MDAKB2_Ant	cytotoxicity burst EDSP AR				263	1771			Inactive	-	1.26	1.00e-4	-4.00	20.00	
UPITT_HCI_U2OS_AR_TIF2_N	EDSP AR		P10275.3	AR	23	25			Inactive	-	11.75	3.10e-2	-1.51	37.98	
TOX21_AR_BLA_Antagonist_v	cytotoxicity burst EDSP AR				263	1771			Inactive	-	2.66	9.27e-3	-2.03	23.06	
OT_AR_ARSRC1_0960	EDSP AR		P10275.3 NP_005408.1	AR | SRC	23	25			Inactive	0	1.94	94.83	1.98	20.00	
TOX21_AR_LUC_MDAKB2_Ant	EDSP AR		P10275.3	AR	-	-			Inactive	0	1.22e-8	45.00	1.65	32.13	
OT_AR_ARSRC1_0480	EDSP AR		P10275.3 NP_005408.1	AR | SRC	23	25			Inactive	0	2.62e-11	50.00	1.70	20.00	
UPITT_HCI_U2OS_AR_TIF2_N	EDSP AR		P10275.3	AR	23	25			Inactive	0	1.01e-10	50.00	1.70	20.00	
TOX21_AR_LUC_MDAKB2_Ag	EDSP AR		P10275.3	AR	23	25			Inactive	-	0.47	7.49e-3	-2.13	20.00	
ATG_AR_TRANS	EDSP AR		P10275.3	AR	-	-			Inactive	0	4.60e-11	100.00	2.00	0.86	



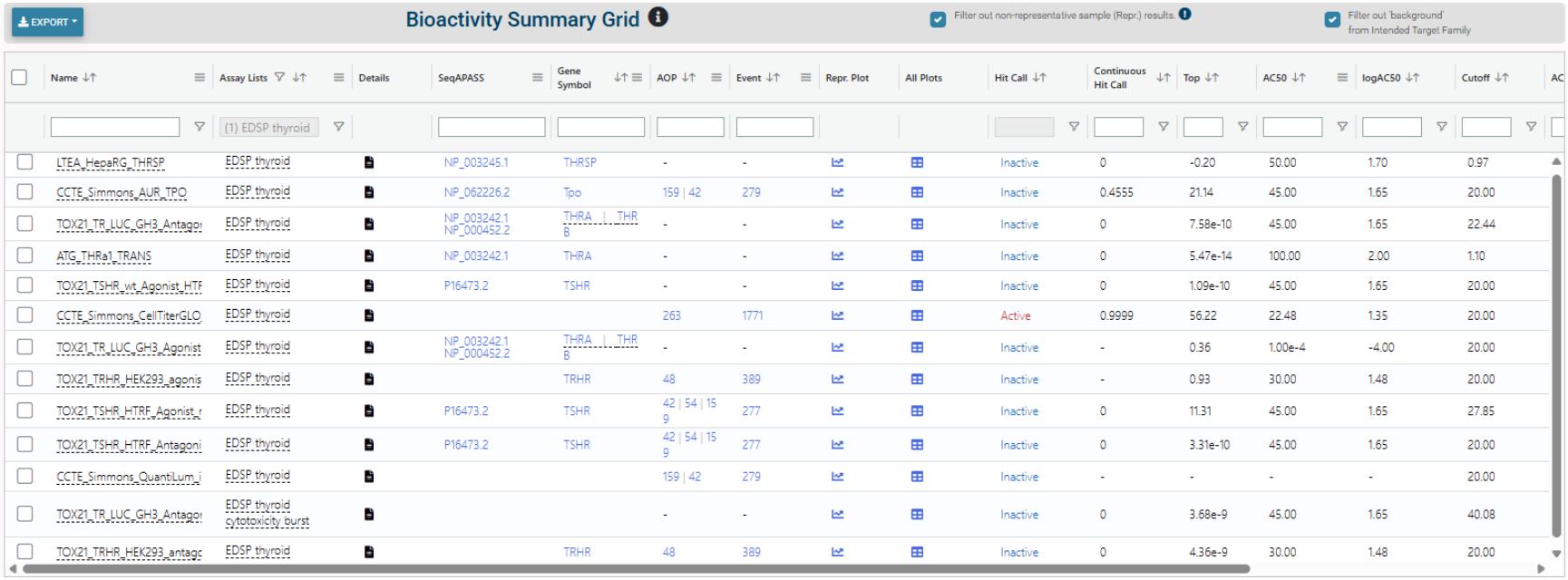
EXPORT

Bioactivity Summary Grid

Filter out non-representative sample (Repr.) results

Filter out 'background' from Intended Target Family

Name	Assay Lists	Details	SeqAPASS	Gene Symbol	AOP	Event	Repr. Plot	All Plots	Hit Call	Continuous Hit Call	Top	AC50	logAC50	Cutoff	AC
	(1) EDSP steroido														
TOX21_Aromatase_Inhibition	EDSP steroidogenesis		NP_000094.2	CYP19A1	25	36			Inactive	0	3.82	45.00	1.65	26.84	-
TOX21_Aromatase_Inhibition_	cytotoxicity burst EDSP steroidogenesis				25 | 263	36 | 1771			Inactive	0	4.02e-9	45.00	1.65	27.62	-



EXPORT

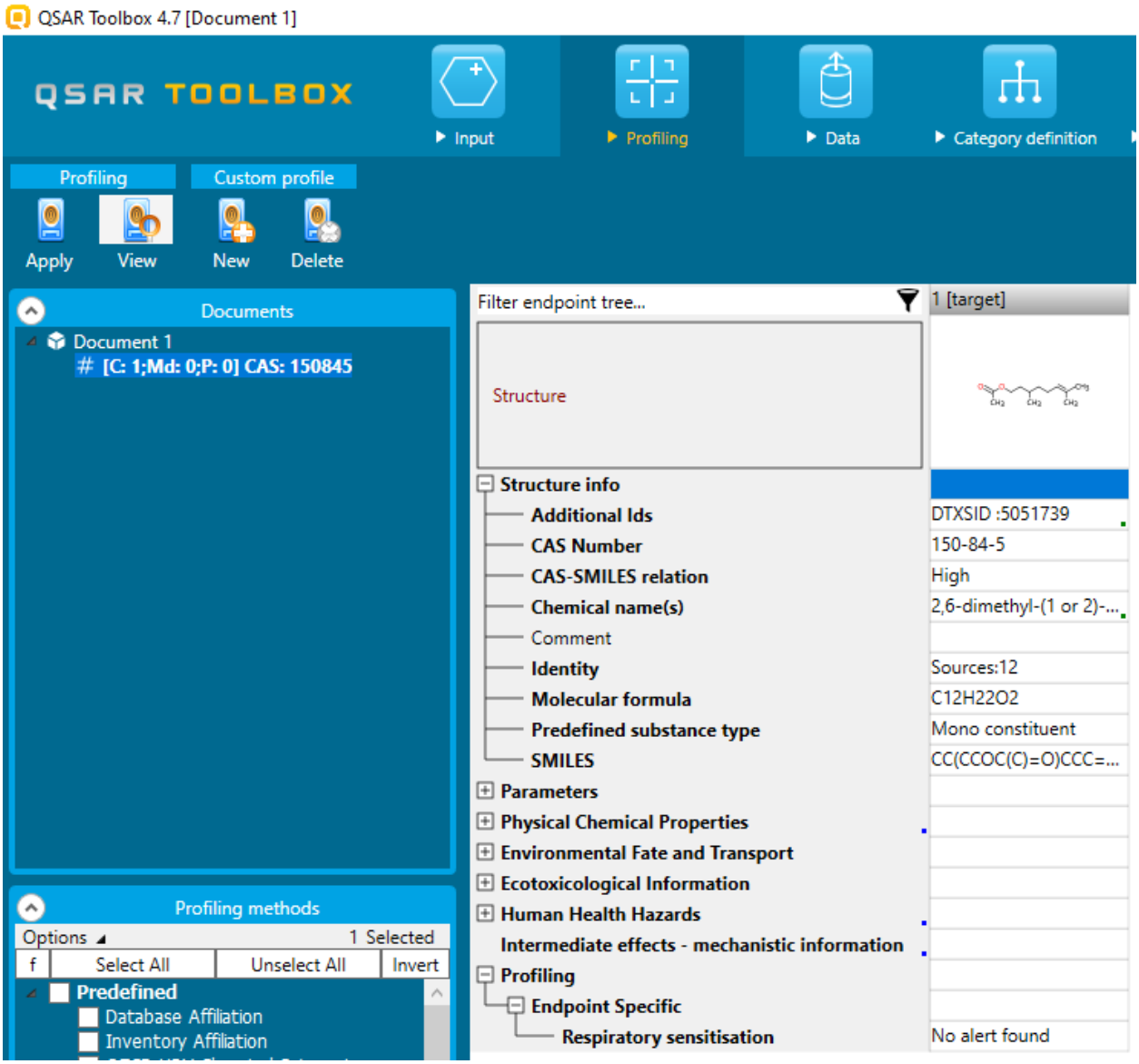
Bioactivity Summary Grid

Filter out non-representative sample (Repr.) results

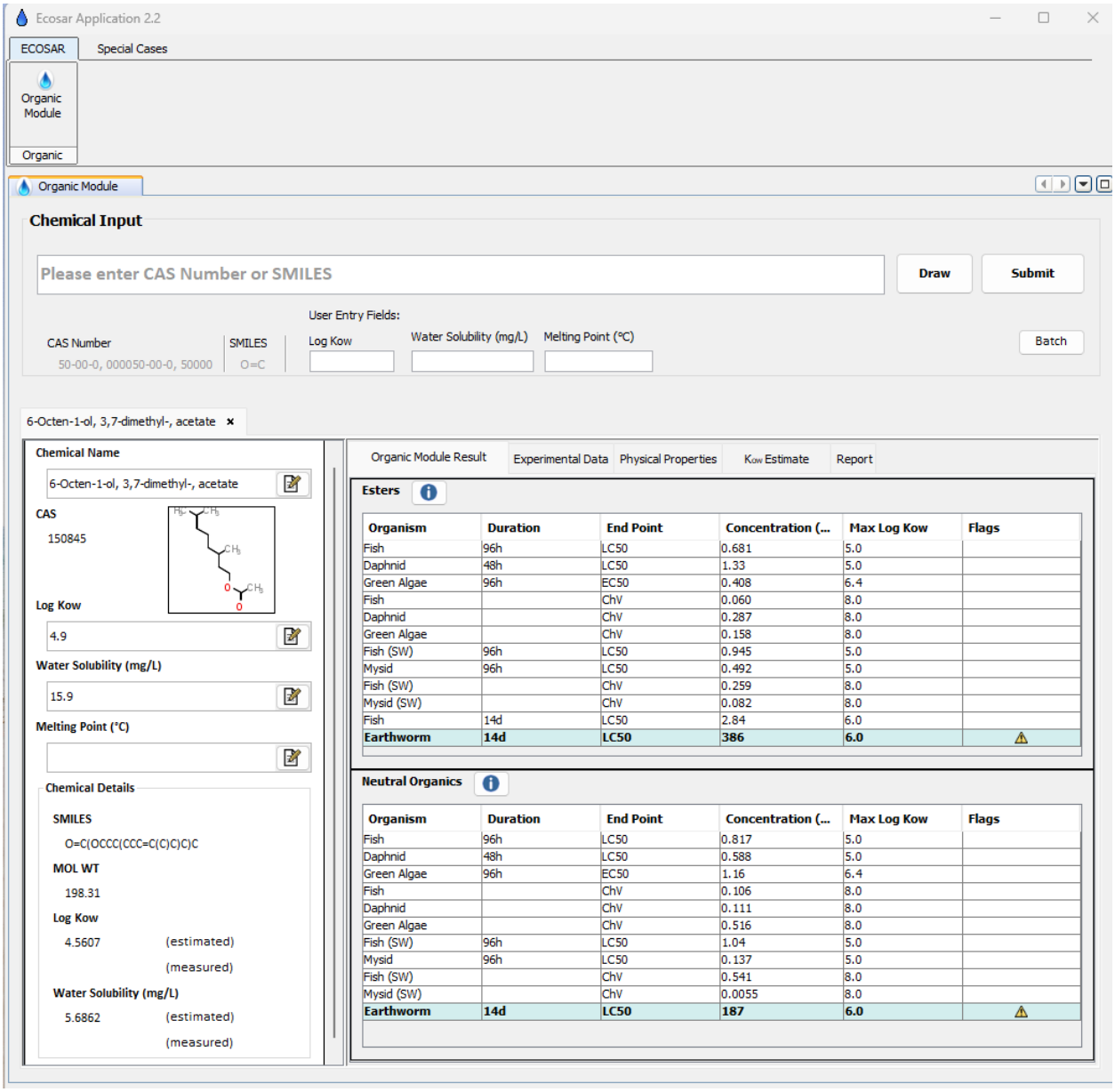
Filter out 'background' from Intended Target Family

Name	Assay Lists	Details	SeqAPASS	Gene Symbol	AOP	Event	Repr. Plot	All Plots	Hit Call	Continuous Hit Call	Top	AC50	logAC50	Cutoff	AC
	(1) EDSP thyroid														
LTEA_HepaRG_THRSP	EDSP thyroid		NP_003245.1	THRSP	-	-			Inactive	0	-0.20	50.00	1.70	0.97	
CCTE_Simmons_AUR_TPO	EDSP thyroid		NP_062226.2	Tpo	159 | 42	279			Inactive	0.4555	21.14	45.00	1.65	20.00	
TOX21_TR_LUC_GH3_Antagor	EDSP thyroid		NP_003242.1 NP_000452.2	THRA | THRB	-	-			Inactive	0	7.58e-10	45.00	1.65	22.44	
ATG_THRa1_TRANS	EDSP thyroid		NP_003242.1	THRA	-	-			Inactive	0	5.47e-14	100.00	2.00	1.10	
TOX21_TSHR_wt_Agonist_HTF	EDSP thyroid		P16473.2	TSHR	-	-			Inactive	0	1.09e-10	45.00	1.65	20.00	
CCTE_Simmons_CellTiterGLO	EDSP thyroid				263	1771			Active	0.9999	56.22	22.48	1.35	20.00	
TOX21_TR_LUC_GH3_Agonist	EDSP thyroid		NP_003242.1 NP_000452.2	THRA | THRB	-	-			Inactive	-	0.36	1.00e-4	-4.00	20.00	
TOX21_TRHR_HEK293_agonis	EDSP thyroid			TRHR	48	389			Inactive	-	0.93	30.00	1.48	20.00	
TOX21_TSHR_HTRF_Agonist_r	EDSP thyroid		P16473.2	TSHR	42 | 54 | 159	277			Inactive	0	11.31	45.00	1.65	27.85	
TOX21_TSHR_HTRF_Antagoni	EDSP thyroid		P16473.2	TSHR	42 | 54 | 159	277			Inactive	0	3.31e-10	45.00	1.65	20.00	
CCTE_Simmons_QuantiLum_i	EDSP thyroid				159 | 42	279			Inactive	-	-	-	-	20.00	
TOX21_TR_LUC_GH3_Antagor	EDSP thyroid cytotoxicity burst				-	-			Inactive	0	3.68e-9	45.00	1.65	40.08	
TOX21_TRHR_HEK293_antago	EDSP thyroid			TRHR	48	389			Inactive	0	4.36e-9	30.00	1.48	20.00	

APPENDIX D: OECD Toolbox Respiratory Sensitization Results for Surrogate Citronellyl Acetate (CAS #150-84-5)

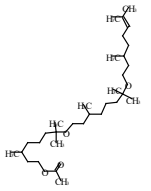


APPENDIX E: ECOSAR Modeling Results for Citronellyl Acetate (CAS #150-84-5)



APPENDIX F: EPI Suite™ Modeling Results for Representative Structure of Polycitronellol Acetate (CAS #2417284-25-2)

EPI Suite Results For CAS



```
SMILES : CC(CCCC(C)(C)OCCC(C)CCCC(C)(C)OCCC(C)CCC=C(C)C)CCOC(=O)C
CHEM   :
MOL FOR: C32 H62 O4
MOL WT : 510.85
---------------------------- EPI SUMMARY (v4.11) -------------------------
Physical Property Inputs:
Log Kow (octanol-water):   ------
Boiling Point (deg C)  :   ------
Melting Point (deg C)  :   ------
Vapor Pressure (mm Hg) :   ------
Water Solubility (mg/L):   ------
Henry LC (atm-m3/mole) :   ------

Log Octanol-Water Partition Coef (SRC):
Log Kow (KOWWIN v1.69 estimate) =  11.50

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
Boiling Pt (deg C):  480.18  (Adapted Stein & Brown method)
Melting Pt (deg C):  185.77  (Mean or Weighted MP)
VP(mm Hg,25 deg C):  1.81E-009  (Modified Grain method)
VP (Pa, 25 deg C) :  2.42E-007  (Modified Grain method)
Subcooled liquid VP: 8.67E-008 mm Hg (25 deg C, Mod-Grain method)
: 1.16E-005 Pa (25 deg C, Mod-Grain method)

Water Solubility Estimate from Log Kow (WSKOW v1.42):
Water Solubility at 25 deg C (mg/L):  9.206e-008
log Kow used: 11.50 (estimated)
no-melting pt equation used

Water Sol Estimate from Fragments:
Wat Sol (v1.01 est) =  7.6208e-006 mg/L

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

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
```

```
Bond Method :   5.24E-005  atm-m3/mole  (5.31E+000 Pa-m3/mole)
Group Method:   1.31E-006  atm-m3/mole  (1.33E-001 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:  1.322E-002 atm-m3/mole  (1.339E+003 Pa-m3/mole)
VP:   1.81E-009 mm Hg (source: MPBPVP)
WS:   9.21E-008 mg/L (source: WSKOWWIN)

Log Octanol-Air Partition Coefficient (25 deg C) [KOAWIN v1.10]:
Log Kow used:  11.50  (KowWin est)
Log Kaw used:  -2.669  (HenryWin est)
Log Koa (KOAWIN v1.10 estimate):  14.169
Log Koa (experimental database):  None

Probability of Rapid Biodegradation (BIOWIN v4.10):
Biowin1 (Linear Model)         :  -0.3841
Biowin2 (Non-Linear Model)     :   0.0000
Expert Survey Biodegradation Results:
Biowin3 (Ultimate Survey Model):   1.7689  (months      )
Biowin4 (Primary Survey Model) :   3.0133  (weeks       )
MITI Biodegradation Probability:
Biowin5 (MITI Linear Model)    :   0.2757
Biowin6 (MITI Non-Linear Model):   0.0157
Anaerobic Biodegradation Probability:
Biowin7 (Anaerobic Linear Model): -1.1780
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):  1.16E-005 Pa (8.67E-008 mm Hg)
Log Koa (Koawin est  ): 14.169
Kp (particle/gas partition coef. (m3/ug)):
Mackay model           :  0.26
Octanol/air (Koa) model:  36.2
Fraction sorbed to airborne particulates (phi):
Junge-Pankow model     :  0.904
Mackay model           :  0.954
Octanol/air (Koa) model:  1

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant = 139.9894 E-12 cm3/molecule-sec
Half-Life =     0.076 Days (12-hr day; 1.5E6 OH/cm3)
Half-Life =     0.917 Hrs
Ozone Reaction:
OVERALL Ozone Rate Constant =    43.000000 E-17 cm3/molecule-sec
Half-Life =     0.027 Days (at 7E11 mol/cm3)
Half-Life =     38.378 Min
Reaction With Nitrate Radicals May Be Important!
Fraction sorbed to airborne particulates (phi):
0.929 (Junge-Pankow, Mackay avg)
1 (Koa method)
Note: the sorbed fraction may be resistant to atmospheric oxidation
```

```
Soil Adsorption Coefficient (KOCWIN v2.00):
Koc    :  1.891E+006  L/kg (MCI method)
Log Koc:  6.277       (MCI method)
Koc    :  1.095E+007  L/kg (Kow method)
Log Koc:  7.039       (Kow method)

Aqueous Base/Acid-Catalyzed Hydrolysis (25 deg C) [HYDROWIN v2.00]:
Total Kb for pH > 8 at 25 deg C :  1.025E-001  L/mol-sec
Kb Half-Life at pH 8:      78.232  days
Kb Half-Life at pH 7:       2.142  years
(Total Kb applies only to esters, carbmates, alkyl halides)

Bioaccumulation Estimates (BCFBAF v3.01):
Log BCF from regression-based method = 1.322 (BCF = 21.01 L/kg wet-wt)
Log Biotransformation Half-life (HL) = 1.5984 days (HL = 39.67 days)
Log BCF Arnot-Gobas method (upper trophic) = 0.050 (BCF = 1.121)
Log BAF Arnot-Gobas method (upper trophic) = 2.381 (BAF = 240.4)
log Kow used: 11.50 (estimated)

Volatilization from Water:
Henry LC:  1.31E-006 atm-m3/mole  (estimated by Group SAR Method)
Half-Life from Model River:       1012  hours   (42.19 days)
Half-Life from Model Lake : 1.123E+004  hours   (468.1 days)

Removal In Wastewater Treatment:
Total removal:              94.04  percent
Total biodegradation:        0.78  percent
Total sludge adsorption:    93.26  percent
Total to Air:                0.00  percent
(using 10000 hr Bio P,A,S)

Level III Fugacity Model: (MCI Method)
** Note: When the Log Kow is > 7, the model may be underestimating
the mass of material in sediment and overestimating the mass of
material in the water column (biota). Consider using the results
of the default EQC model. **

Mass Amount    Half-Life    Emissions
(percent)        (hr)       (kg/hr)
Air       0.0136          0.474        1000
Water     13.8            1.44e+003    1000
Soil      86.1            2.88e+003    1000
Sediment  0.132           1.3e+004     0
Persistence Time: 1.64e+003 hr

Level III Fugacity Model: (MCI Method with Water percents)
Mass Amount    Half-Life    Emissions
(percent)        (hr)       (kg/hr)
Air       0.0136          0.474        1000
Water     13.8            1.44e+003    1000
water     (0.000871)
biota     (13.8)
suspended sediment (0.00247)
Soil      86.1            2.88e+003    1000
Sediment  0.132           1.3e+004     0
Persistence Time: 1.64e+003 hr
```

Level III Fugacity Model: (EQC Default)

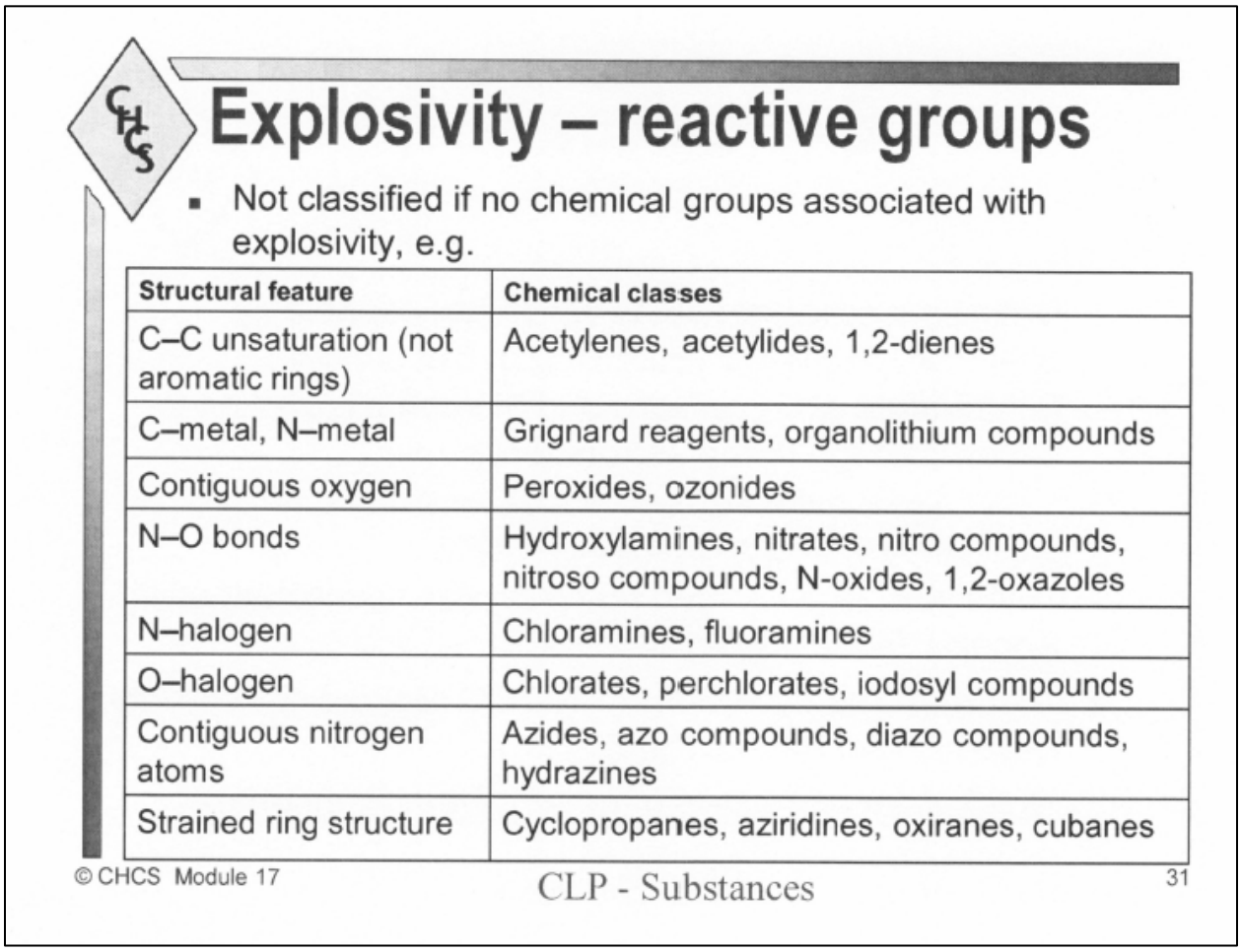
Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)	
Air	0.00473	0.474	1000
Water	1.39	1.44e+003	1000
water	(6.6e-006)		
biota	(0.104)		
suspended sediment	(1.28)		
Soil	29.9	2.88e+003	1000
Sediment	68.7	1.3e+004	0

Persistence Time: 4.7e+003 hr

....

APPENDIX G: Known Structural Alerts for Reactivity

Explosivity – Abbreviated List



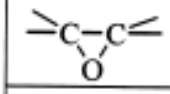
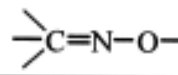
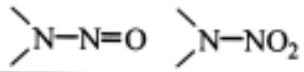
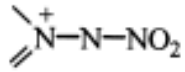
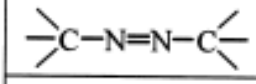
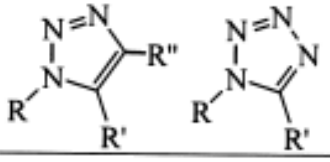
Explosivity – reactive groups

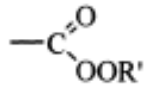
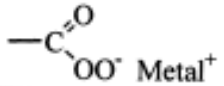
- Not classified if no chemical groups associated with explosivity, e.g.

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

Explosivity – Full List

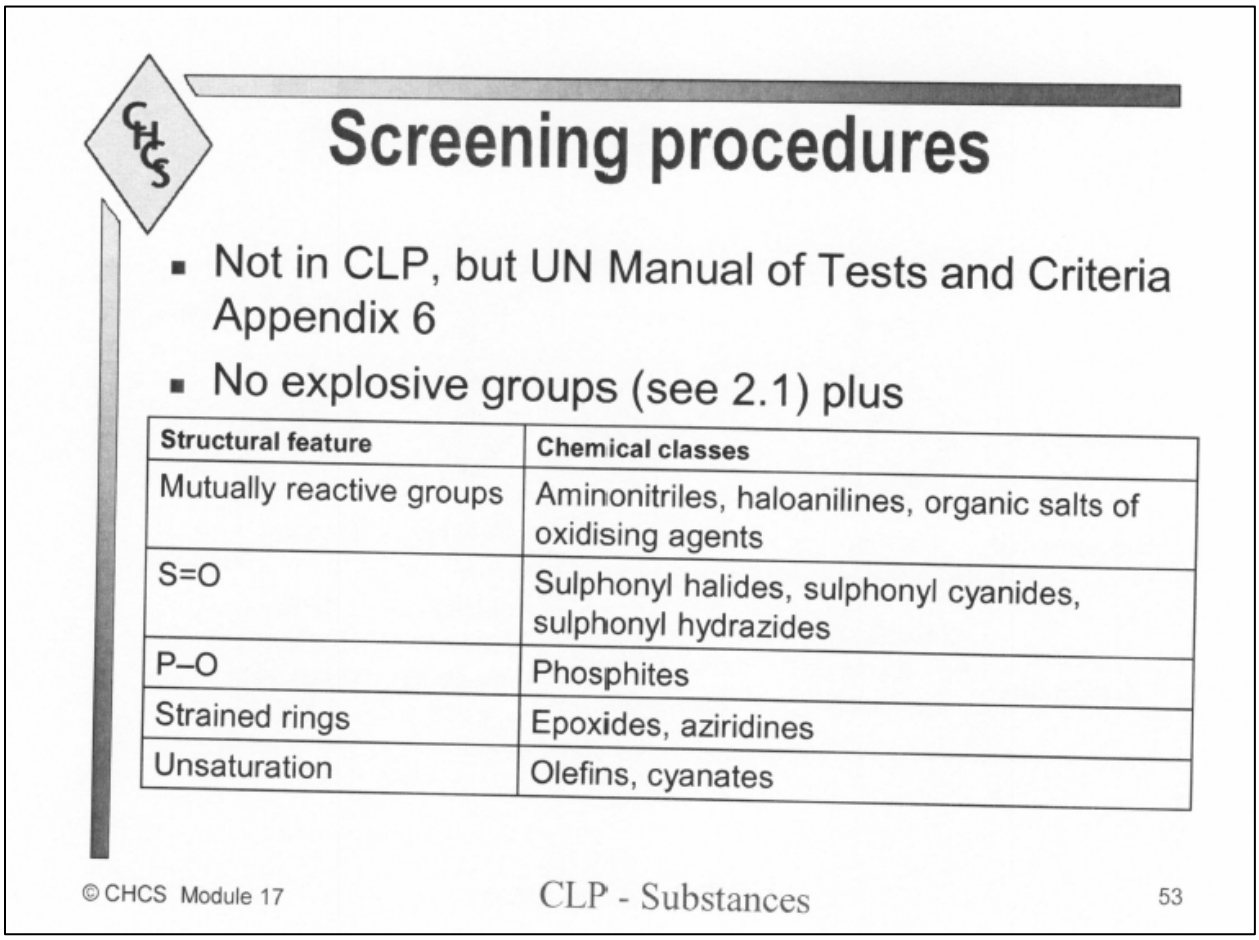
Table R.7.1-28 Chemical groups associated with explosive properties

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. NCl_3, $RNCl_2$	N-Halogen Compounds

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

Self-Reactive Substances



APPENDIX H: Change in Benchmark Score

Table 5 provides a summary of changes to the GreenScreen® Benchmark™ for polycitronellol acetate. The original GreenScreen® assessment was performed in March 2025 under version 1.4 criteria and ToxServices assigned a Benchmark 2 (BM-2) score.

Table 5: Change in GreenScreen® Benchmark™ for Polycitronellol Acetate

Date	GreenScreen® Benchmark™	GreenScreen® Version	Comment
March 21, 2025	BM-2	v. 1.4	Original GreenScreen® assessment.
July 9, 2025	BM-2	v. 1.4	Minor edits made to correct typos and strengthen score justifications. No change in BM score.

Licensed GreenScreen® Profilers

Polycitronellol Acetate GreenScreen® Evaluation Prepared by:

SIGNATURE BLOCK

Mitchell Kelly, M.S.
Toxicologist
ToxServices LLC

Polycitronellol Acetate GreenScreen® Evaluation QC'd by:

SIGNATURE BLOCK

Margaret H. Whittaker, Ph.D., M.P.H., CBiol., F.R.S.B., E.R.T., D.A.B.T.
Managing Director and Chief Toxicologist
ToxServices LLC

SIGNATURE BLOCK

Bingxuan Wang, Ph.D., D.A.B.T.
Senior Toxicologist
ToxServices LLC